JOURNAL OF
The American Geriatrics Society

Volume IV *July 1956* Number 7

CONTENTS

Massive Prednisone and Prednisolone Therapy in Leukemia and Lymphomas in the Adult. *Joseph M. Hill, G. J. Marshall and Dalcio J. Falco* 627

Problems of Geriatric Care. *Joseph H. Sheldon* 642

Management of Foot Lesions in the Elderly Diabetic. *David Hurwitz* 648

Mortality Among the Married. *Dewey Shurtleff* 654

Electrophoretic Serum Protein Patterns in the Aged. *J. L. Karel, V. M. Wilder and M. Beber* 667

Host-Tumor Antagonism. I. Evidence for the Existence of "Tumor Immunity." *Louis Pelner* 683

Nurse-Patient Relationships. *Beatrix Cobb, M. Catherine Asher, Mabel Embrey, Catherine Towey, Estelle Champagne and Marian Metcalf* 690

Care of the Terminal Cancer Patient. *J. Herbert Nagler* 699

Morbidity and Mortality in Old Age. A Study of Experience in a Modern Home for the Aged. Part II. *Israel Gitlitz* 708

Abstracts of Current Literature 722

News and Notices

The National Society for Crippled Children and Adults—Annual Meeting. 731

Ciba's "Medical Horizons" TV Series 731

The American Geriatrics Society

The 1957 Annual Meeting 24

The American Therapeutics Society 25

Index to Advertisers 36

Entered as second-class matter at the Post Office at Baltimore, Md. Subscription price $10.00 per volume. Published monthly.
No part of any article published in this journal may be duplicated or reproduced without permission of the author, publisher and editor.

JOURNAL OF
The American Geriatrics Society

Official Journal of the American Geriatrics Society

EDITOR IN CHIEF
EDWARD HENDERSON

Editor
PHEBE K. THOMPSON

Associate Editor
WALTER E. VEST, JR.

Abstract Editor
GLADYS KOCH WILSON

EDITORIAL BOARD

GEORGE W. AINLAY, SR.
EDWARD B. ALLEN
BROCK E. BRUSH
HOLLIS E. CLOW
WARREN H. COLE
ROBERT ELMAN
FRANK GLENN
GEORGE C. GRIFFITH
NORRIS J. HECKEL
WILLIAM F. HUGHES, JR.
LAURANCE W. KINSELL
WILLIAM B. KOUNTZ
HAROLD W. LOVELL
THOMAS H. MCGAVACK
ROBERT J. PRIEST
CORNELIUS P. RHOADS
LEO T. SAMUELS
HAROLD O. SCHNEIDER
CHARLES T. STONE
RICHARD W. TELINDE
MALFORD W. THEWLIS
MARVIN WEINBERG
MILEY B. WESSON
HAROLD G. WOLFF

Foreign Section

L. BRULL
A. P. THOMPSON

AMERICAN GERIATRICS SOCIETY, Inc.

OFFICERS: *President:* THOMAS H. MCGAVACK, M.D.; *Vice-President:* LAURANCE W. KINSELL, M.D.; *Secretary:* MALFORD W. THEWLIS, M.D.; *Treasurer:* RICHARD J. KRAEMER, M.D.
BOARD OF DIRECTORS: *Chairman,* MALFORD W. THEWLIS, M.D.; EDWARD B. ALLEN, M.D.; HOLLIS E. CLOW, M.D.; EDWARD HENDERSON, M.D.; RICHARD J. KRAEMER, M.D.
Address of the Secretary: MALFORD W. THEWLIS, M.D., 25 Mechanic Street, Wakefield, Rhode Island.

Subscriptions. The *Journal* is published monthly; twelve issues (Jan.–Dec.) constitute a volume. Subscriptions are sold on a volume basis, prorated if back volumes are not available. The subscription price is $10.00 per volume, plus $.75 per volume postage to foreign countries and the Postal Union, and $.25 per volume to Canada. Subscriptions for members of the American Geriatrics Society are included in the annual dues which are $15.00. Single copies, when available, are $1.25 per copy, plus $.25 postage outside the United States. Publisher must be notified 60 days in advance of change of address. Undeliverable journals will be destroyed.

Correspondence relating to remittances for subscriptions, back volumes and advertising should be sent to THE WILLIAMS & WILKINS CO., Mt. Royal & Guilford Aves.. Baltimore 2. Md.

All correspondence concerning editorial matters should be sent to: EDWARD HENDERSON. M.D., 236 Midland Ave., Montclair, N. J.

Correspondence relating to remittances for reprints should be sent to the Waverly Press, Inc., Mt. Royal & Guilford Aves., Baltimore 2, Md.

Correspondence concerning membership applications and membership dues should be sent to: MALFORD W. THEWLIS, M.D., *Secretary,* American Geriatrics Society, 25 Mechanic Street, Wakefield, Rhode Island

No part of any article published in this journal may be duplicated or reproduced without permission of the author, publisher and editor. COPYRIGHT 1956, BY THE AMERICAN GERIATRICS SOCIETY PRINTED IN U.S.A.

JOURNAL OF THE
American Geriatrics Society
Official Journal of the
American Geriatrics Society · American Therapeutic Society · Texas Geriatrics Society

VOLUME IV *July. 1956* NUMBER 7

MASSIVE PREDNISONE AND PREDNISOLONE THERAPY IN LEUKEMIA AND LYMPHOMAS IN THE ADULT*†

JOSEPH M. HILL, M.D., G. J. MARSHALL, PH.D. AND DALCIO J. FALCO, M.D.

Wadley Research Institute and Blood Center and the Hematologic Service of Baylor University Hospital, Dallas, Texas

Most investigators agree that acute leukemia in the adult is more difficult to treat than acute leukemia in the child. Bross (1), for example, in his statistical analysis of results of mercaptopurine therapy, noted that children do better than adults; the rank *t*-test yielded the highly significant result of 14.1, derived from Burchenal's series of 89 children and 49 adults. The folic-acid antagonists ("antimetabolites") likewise have been more effective in children than in adults, as shown by Stickney (2), Burchenal (3), and Scott (4). Cortisone or corticotropin therapy has been followed by a higher remission rate than has antimetabolic treatment; moreover the onset of remission is more rapid, though of shorter duration. Again the results have been better in children (4, 5, 6). Wintrobe *et al.* (7) stated that hormone therapy is contraindicated in acute granulocytic and monocytic leukemia—types which are relatively much more common in the adult. Recent reports on results of treatment in large series of cases of acute leukemia have been most pessimistic, especially with respect to survival time (4, 5, 8). Scott (4) and Haut *et al.* (5) were unable to find statistically significant differences in survival of treated and untreated cases of acute leukemia.

Bernard and Deltour (9) in 1953 reported good results from the use of massive doses of cortisone (1 gram) repeated twice weekly for four to six weeks. Later, single doses as high as 5 grams in one day were found effective in producing remissions. In 1955, Hill and Vincent (10, 11) reported the results of massive and sustained therapy with 9-alpha-fluorohydrocortisone in 14 cases of acute leukemia; there was complete remission in 7 cases and partial remission in 3. Dosages ranged up to 400 mg. daily. Later this series was increased to 21 cases; there were 9 complete and 4 partial remissions, with a maximum dosage

* Presented at the Graduate Symposium on Geriatric Medicine of the American Geriatrics Society, New York, N. Y., November 30 and December 1, 1955.

† The authors wish to thank the Clinical Research Division, Schering Corporation, Bloomfield, New Jersey, for generous supplies of prednisone (Meticorten) and prednisolone (Meticortelone) used in these studies.

TABLE 1

Summary of Results in 19 Patients Over 30 Years of Age

Patient			Diagnosis	Symptoms	Physical Findings	Blasts		Dosage of Prednisolone or Prednisone (mg.)	Prior to Therapy						Following Therapy						Comments
									Blood			Marrow			Blood			Marrow			
No. and init.	Age (yrs.)	Sex				Blood	Marrow		Platelet Count	WBC	Blasts	Cellularity	Blasts	R/W	Platelets	WBC	Blasts	Cellularity	Blasts	R/W	
Acute Leukemia																					
						%	%				%		%				%		%		
1. M. H.	81	F	Monocytic	Weakness; fatigue	Anemia; lymphadenopathy; hepatomegaly	66	32	48,950 in 20 days	572,000	76,600	66	Slightly decreased	32	12/88	163,200	11,000	0.0	Hypoplastic	8.5	6/94	Complete remission; hypoplastic picture.
2. A. H.	34	F	Monocytic	Pelvic, low-back and joint pains; fever	Anemia; slight scoliosis; thrombocytopenia	33	34	18,690 in 23 days	82,700	13,700	33	Hypoplastic	69	5/95	319,200	7,300	0.0	Hypoplastic	24.0	29/71	Partial remission; rapid relief of bone and joint pains. Rapid erythroid response.
3. T. R.	62	M	Granulocytic	Malaise; weakness; fever	Subcut. abscess of rt. neck; anemia; thrombocytopenia	75	96	31,290 in 28 days	55,400	30,500	89	Hyperplastic	96	2/98	36,000	2,500	0.0	Slightly hypoplastic	9.0	1/99	Complete remission, when combined with MP* therapy. Rapid healing of the abscess prior to the initiation of MP.
4. E. B.	52	M	Granulocytic	Weakness; backache; headache; fever; ulcers of mouth	Hepatomegaly; splenomegaly; anemia; thrombocytopenia	81	54	25,875 in 18 days	22,800	500	12	Normal	0	24/76	4,700	5,100	0.0				Partial remission, when combined with MP. A second trial of massive steroid dosage was without apparent benefit.
5. A. H.	66	M	Granulocytic, subacute, becoming acute	Fever; chills; severe pain in rt. leg	Anemia; thrombocytopenia	20	15	12,000 in 6 days	86,800	98,200	82				70,500	114,000	80.0				No improvement with massive prednisone therapy and no definite remission with antimetabolites.
6. E. R.	41	M	Granulocytic	Weakness; fatigue; pharyngitis; stomatitis	Hepatomegaly; splenomegaly; ecchymoses; anemia; thrombocytopenia	64	37	20,260 in 15 days	10,600	86,900	64	Hyperplastic	38	2/98	3,900	10,800	80.0				No improvement with massive steroid therapy, alone or in combination with AME† or MP. Leukocytes were depressed but the % of myeloblasts was increased.

7. C. G.	69	M	Granulocytic	Sinusitis; pharyngitis	Hepatomegaly; splenomegaly; thrombocytopenia; ecchymoses	12	14	49,450 in 22 days	2,400	5,700	0	Normal	41	2/98	1,700	7,700	1.0				Liver and spleen decreased in size with clinical improvement. Afebrile only during massive prednisolone therapy. Persistent thrombocytopenia.
8. A. N.	35	M	Granulocytic	Fatigue; weakness; hemorrhage	Lymphadenopathy; ulceration of mouth; thrombocytopenia	17	—	25,020 in 12 days	21,300	2,500	17				14,800	45,400	94.0				Rapid progression of leukemia Therapy without effect.
9. F. H.	47	M	Granulocytic	Weakness; epistaxis	Hepatomegaly; splenomegaly; thrombocytopenia; anemia	46	62	15,355 in 14 days	49,400	8,800	46	Hyperplastic	62	3/97	3,600	3,300	12	Hypoplastic	3.0	5/95	Rapid initial reduction of blasts when massive steroid therapy was combined with MP. Complete remission.
10. L. B.	47	F	Granulocytic, chronic, becoming acute	Weakness; weight loss	Splenomegaly	3	0	43,000 in 11 days	273,000	127,000	92				19,100	224,000	97.0				No effect on the terminal explosive myeloblastic proliferation.
11. S. H.	30	M	Lymphocytic	Fatigue; abdominal fullness	Lymphadenopathy; thrombocytopenia	72	61	28,120 in 9 days	51,600	384,000	71				6,600	5,200	66.0				Marked decrease in leukocytes and hepato-splenomegaly. No decrease in lymphoblasts.
12. N. M.	51	F	Lymphocytic	Fatigue; weakness; nausea; dyspnea	Lymphadenopathy; splenomegaly; hepatomegaly; thrombocytopenia	0	61	38,725 in 27 days	126,000	61,000	0	Normal	61	4/96	86,000	6,800	0.0	Hypocellular	0.0	7/93	A complete remission; marked psychotic effects, which were completely reversed with convulsant therapy.

TABLE 1—*Continued*

Patient			Diagnosis	Symptoms	Physical Findings	Lymphocytes		Dosage of Prednisolone or Prednisone (mg.)	Prior to Therapy						Following Therapy						Comments
									Blood			Marrow			Blood			Marrow			
No. and init.	Age (yrs.)	Sex				Blood	Marrow		Platelet Count	WBC	Lymphocytes	Lymph nodes	Spleen	Liver	Platelets	WBC	Lymphocytes	Lymph nodes	Spleen	Liver	
Chronic Leukemia and Lymphoma																					
						%	%				%						%				
13. N. M.	74	M	Chronic lymphocytic leukemia	Weakness	Anemia; massive lymphadenopathy; edema of legs	94	—	21,890 in 21 days	171,000	579,000	95	10	3		63,800	450,800	96	4	1		Rapid reduction in size of lymph nodes with disintegration of leukemic cells, but no significant reduction in the leukocyte count; platelets depressed.
14. O. S.	46	M	Chronic lymphocytic leukemia		Lymphadenopathy; splenomegaly; hepatomegaly; thrombocytopenia; anemia	97	—	20,103 in 17 days	28,800	8,800	65	5	1	4	30,200	5,500	56	5	1		No appreciable effect of massive prednisolone therapy on the progress of leukemia, or the hemolytic component.
15. T. S.	72	M	Chronic lymphocytic leukemia	Weakness; anorexia; tenderness and soreness of R.U.Q.	Thrombocytopenia; anemia	88	69	13,499 in 25 days	138,800	34,600	88	0	0	0	582,500	10,100	40	0	0	0	Good remission, with a marked decrease in lymphocytes in blood and marrow. Patient has been maintained without further therapy.
16. C. H.	44	M	Chronic lymphocytic leukemia	Pharyngitis; dizziness	Lymphadenopathy; splenomegaly; edema	88	—	30,450 in 23 days	75,000	40,700	83	7	—	3	17,100	10,700	99	2	—	3	Marked and rapid decrease of bilat. cerv. and axill. lymphadenopathy. Pneumonia developed—perhaps related to prolonged steroid therapy.

17. B. S.	53	F	Giant follicular lymphoblastoma	Nausea; fever; weakness	Lymphadenopathy; splenomegaly; edema	66	40	6,100 in 9 days	407,700	10,800	66	10	4	3	481,400	45,800	58	4	0	0	Remarkable decrease in lymph nodes, liver and spleen. Leukocytes increased until radioisotope therapy was initiated. Patient now maintained without treament.
18. R. H.	44	M	Reticulum-cell sarcoma	Fever; pain in rt. leg	Rt. leg edematous, with large red areas			33,285 in 32 days	236,000	8,000	13				161,000	2,500	18	0	0	0	Reduction in size of the inguino-abdom. mass with prednisolone, following resistance to irradiation. Slight leukocytosis.
19. C. V.	56	M	Lymphosarcoma	Weakness; leg cramps	Lymphadenopathy; hepatomegaly; splenomegaly; thrombocytopenia	34		11,735 in 68 days	90,200	5,300	29	5	7	7	155,000	4,500	27	1	2	4	Liver, spleen and lymph nodes were markedly reduced in size, when combined with TEM.‡ Platelets decreased, but increased when steroid was discontinued.

* Mercaptopurine.

† Antimetabolites, such as amethopterin.

‡ Triethylenemelamine.

of 600 mg. daily. Four of these patients who experienced remission were over 30 years of age and had acute granulocytic leukemia. In 1 patient aged 66, with classic plasma-cell leukemia, there was a complete remission.

Because administration of fluorohydrocortisone required close observation of sodium and potassium levels and the administration of as much as 100 mEq. of potassium daily, trials with other steroids were continued. This report, therefore, is concerned with an analysis of results of massive prednisone and prednisolone therapy in 12 cases of acute leukemia, 4 cases of chronic lymphocytic leukemia, and 3 cases of lymphoma. Although many other patients were treated with steroids, only those receiving over 250 mg. daily are included in the study, since massive dosage was employed in almost every instance when a remission was being sought. Lesser amounts of steroids were used as adjuvant therapy to antimetabolites, for such purposes as stimulation of platelet production.

From our earlier experience with massive steroid therapy in acute leukemia, this form of treatment seemed to be most useful 1) in the acutely ill patient, a circumstance in which there is little time to wait for the effect of the slower-acting antimetabolites; 2) in the patient failing to respond to adequate antimetabolic therapy; and 3) in the patient who, late in the disease, has apparently lost the ability to respond to all forms of treatment. These three categories became the criteria for massive steroid therapy. A few other patients with leukemia were added during the study, in whom this treatment was considered optional. In every instance, the overall therapy was individualized to fit the needs of the patient. Blood transfusion was used freely, preferably before specific therapy. Antibiotics (up to a combination of four) were used in accord with the results of sensitivity testing whenever material was available for culture. Stool, sputum and blood cultures were found most useful. If antibiotics were required prior to reports of the sensitivity tests, these drugs were chosen on the basis of data collected from previous testing in leukemia. In addition to the general score of the antibiotics, the probable type of organism, according to the location of infection when known or suspected, was taken into account. Antihemorrhagic measures likewise were employed, on the basis of previous studies of the coagulation defect in leukemia. These measures included the use of fresh blood, platelet concentrates, vitamin K_1, vitamin C, bioflavonoids and the steroids themselves. Combined therapy was never denied the patient when the addition of an antimetabolite was considered necessary to obtain a remission. The tendency of folic-acid antagonists to depress platelet formation, and of mercaptopurine to depress leukocyte levels was kept in mind.

A brief summary of 19 cases is presented in Table 1. Only those patients over 30 years of age were included. However, patients of all ages were included in the broader background of analyzed results of 121 cases of acute leukemia seen in the five years prior to 1955. The following are summaries of the case histories of 4 of the 19 patients listed in Table 1:

Case 1—M. H. Acute Monocytic Leukemia (Fig. 1)

This 81-year-old woman became weak and easily fatigued in August 1955. Several weeks later she was hospitalized for a general checkup and, after preliminary studies, was re-

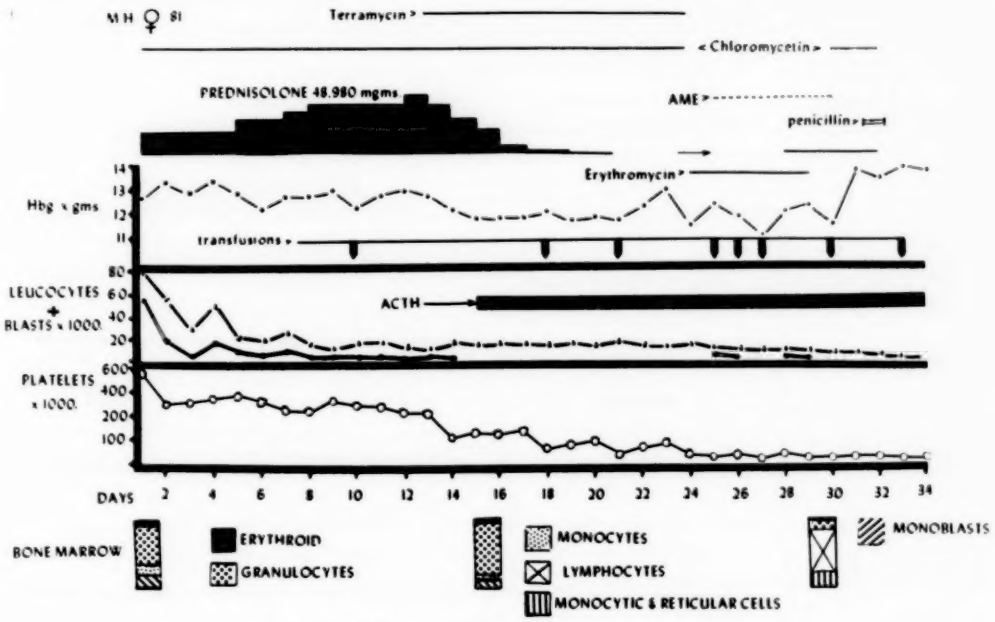

FIG. 1. Case 1. Acute monocytic leukemia.

ferred to our service for further diagnostic and therapeutic procedures. The only significant physical findings were moderate cervical and inguinal lymphadenopathy and hepatomegaly. The leukocyte count was 76,600, with 66 per cent monoblasts. The bone marrow was hypoplastic, with a decrease in the myeloid and erythroid elements; 32 per cent of the cell were monoblasts and 15 per cent monocytes—most of them immature. She was given 48,950 mg. of prednisolone in twenty days, the maximum dosage being 5 grams in one day. When the drug was discontinued, the leukocyte count was 11,000; the monoblasts had disappeared entirely from the peripheral blood and had decreased to less than 10 per cent in the marrow. The marrow was still hypoplastic and showed 12.5 per cent cells of the reticular type. This patient was also given chloramphenicol during the entire period of steroid therapy. Frequent blood sugar, potassium and sodium determinations were made during and after the prednisolone therapy. The sodium level was normal throughout. The blood sugar level varied from 168 mg. per 100 cc. in the initial phase of therapy to 153 mg. per 100 cc. later. Surprisingly, potassium concentration tended to run high (from 5.1 to a maximum of 6.2 mEq. per liter). Oral potassium chloride had been given because of the high dosage of prednisolone.

This case is of interest because of the age of the patient and the high dosage of the steroid. A complete remission was obtained with respect to disappearance of the monoblasts, but not with respect to the hypoplastic picture. The high serum potassium level shows the danger of excessive potassium administration and indicates the striking difference in this respect between prednisolone and the earlier steroids.

Case 3—T. R. Acute Granulocytic Leukemia (Fig. 2)

This 62-year-old man was seen on our service April 4, 1955. He had pneumonia in December 1954, followed by malaise, weakness and intermittent fever. In March 1955, his local physician made a diagnosis of leukemia and referred him here for treatment. At that time leukocyte count was 19,100, with 75 per cent myeloblasts, the hemoglobin level

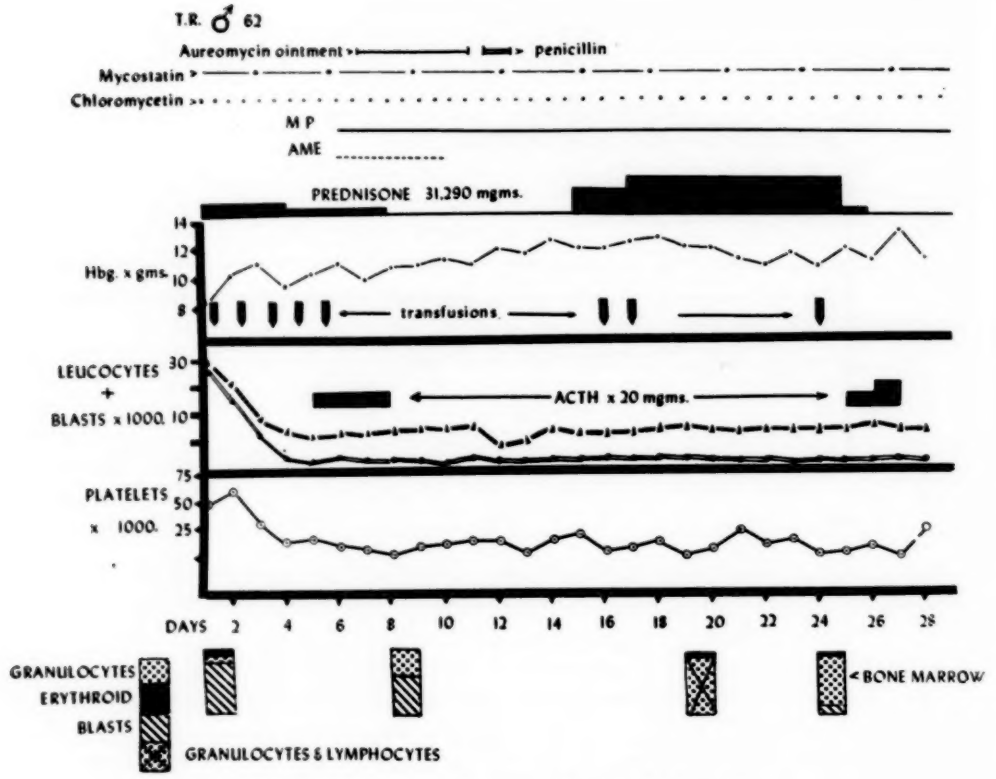

FIG. 2. Case 3. Acute granulocytic leukemia.

was 6 grams, and the platelet count was 42,200. Two days later, the leukocyte count had risen to 30,500. The marrow was hyperplastic, with 96 per cent myeloblasts and no megakaryocytes. After transfusions, prednisone was started in a dosage of 1,000 mg. daily for three days, then decreased to 25 mg. daily. After 3,025 mg. of prednisone had been given, the leukocyte count was 2,100, with only 10 per cent blasts. On the fifth day of therapy, mercaptopurine and amethopterin were added, the former being continued for twenty-four days with a total dosage of 1,600 mg., and the latter for four days with a total dosage of 17.5 mg. On the fifteenth day, prednisolone therapy was increased to massive dosage (2 to 3 grams daily) for ten days, and then gradually decreased. On the sixth day of this massive therapy the blasts had disappeared from the blood, and from that time until the patient's death five months later, the myeloblasts did not exceed 6 per cent of the leukocyte count. He had no antileukemic therapy from May 6 to May 20. At that time the leukocyte count was 2,100 and platelets had risen to 606,800. Mercaptopurine was given from May 21 to May 25, again in the following month, and again in July and August. He was readmitted to the hospital September 11, 1955, with numerous petechiae on the chest and back. He expired the following day with marked congestion of the chest. The spleen and liver were just palpable. Autopsy showed pulmonary congestion and edema, multiple hemorrhages and slight hepatosplenomegaly.

It is of interest that on this patient's first admission in April 1955, there was a subcutaneous abscess of the right side of the neck over the midportion of the sternomastoid muscle. When the crust was removed, a large necrotic area, one-fourth inch in diameter, was found. This lesion healed during administration of prednisone together with chloromycetin and Mycostatin.

Case 12—N. M. Acute Lymphocytic Leukemia (Fig. 3)

This 51-year-old woman was admitted to the hospital with complaints of fatigue, weakness, nausea, a swollen feeling in the right upper chest, and a dry, wheezing cough—all of about two and a half weeks' duration. Physical examination revealed lymphadenopathy with nodes up to 2.5 cm. in diameter in the left supraclavicular, posterolateral cervical and inguinal regions. There was moderate hepatomegaly and splenomegaly. Signs of fluid were present in the right pleural base up to the midscapular level posteriorly. There was tenderness over the sternum and tibia. The initial leukocyte count was 61,000 with 90 per cent lymphocytes; the hemoglobin level was 12.9 grams, and the platelet count was 126,000. In the bone marrow there was a decrease of megakaryocytes and erythroid elements with an increase of lymphoid forms up to 37.5 per cent. The diagnosis was acute lymphocytic leukemia with some subacute features. The amber colored fluid (700 cc.) removed from the right chest was later shown to be sterile. The patient was afebrile when prednisone, 2 grams daily, was started. The dosage was decreased to 1 gram daily on the sixth day, then increased to 3 grams daily on the fifteenth day and tapered off from the twentieth to the twenty-eighth day. A decrease in the size of the liver, spleen and lymph nodes was noted after six days of prednisone therapy. After ten days of therapy, the spleen was no longer palpable and the lymph nodes were very small. The liver was slightly reduced in size. After about twelve days of therapy, the patient became excitable, talkative, euphoric and hallucinated. At the time of discharge, in remission, her mental disturbance was still present, but it cleared up later. After the attainment of essentially complete remission, a dose of 2 mc. of radiophosphorus was given orally in an effort to sustain it. There was no deviation from normal serum potassium levels and only one abnormally low serum sodium value was noted during the entire hospital stay. The blood sugar level varied from 84 to 185 mg. per 100 cc. Blood pressure showed some irregular elevation during the latter phase of therapy, the systolic pressure varying from 140 to 170, and the diastolic from 80 to 102.

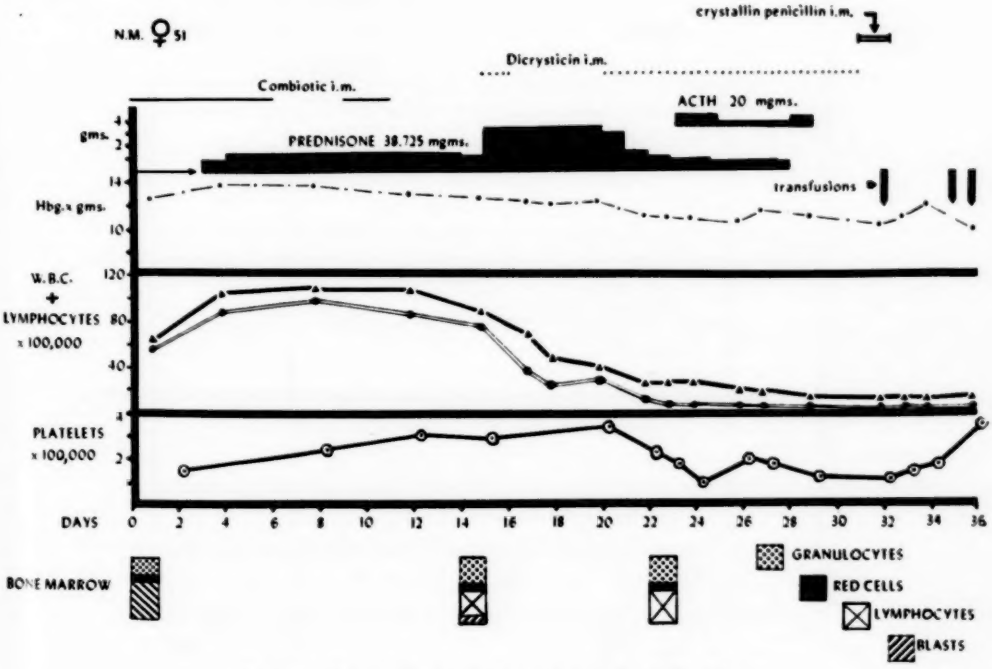

FIG. 3. Case 12. Acute lymphocytic leukemia.

A complete remission during administration of prednisone alone was obtained in this patient, but with the most marked psychotic side-effects seen in the series. This was reversed with convulsant therapy. Platelets were moderately depressed in the tapering-off phase. Moderate but transient elevation of blood pressure and moderate elevation of the blood sugar level occurred during the massive therapy only.

Case 13—N. C. M. Chronic Lymphocytic Leukemia (Fig. 4)

This 74-year-old man was seen September 7, 1955. Four years previously he had noted a slow-growing, soft, nontender mobile mass in the left lateral area of the neck, and there had been an increase in size and quantity of the nodes during this period. When first seen here, the cervical and axillary nodes were enlarged to approximately grapefruit size. The inguinal and abdominal nodes were also enlarged, but were not as prominent. Blood study at this time showed 646,400 leukocytes, 94 per cent of which were lymphocytes. The platelet count was 178,000 and the hemoglobin level was 8.1 grams. Only 1 lymphoblast was noted in the peripheral blood smear. The bone marrow showed marked erythroid and myeloid depression, and lymphocytosis. Megakaryocytes were rare. Prednisolone was started September 9 in a dosage of 3 grams daily for three days, then 75 mg. daily for three days. Further reduction was continued until the fifteenth day, when the patient received 4 grams. On the fifth day of prednisolone therapy, the lymph nodes were only 75 per cent of their former size, and a lymph node biopsy showed a marked dichotomy of cell type. In one area the cells were normal in morphologic characteristics, but in another appeared very fragile, had less affinity for metachromatic dyes, and in general seemed to be disintegrating. At this time there was no reduction in the blood leukocyte count or in the per-

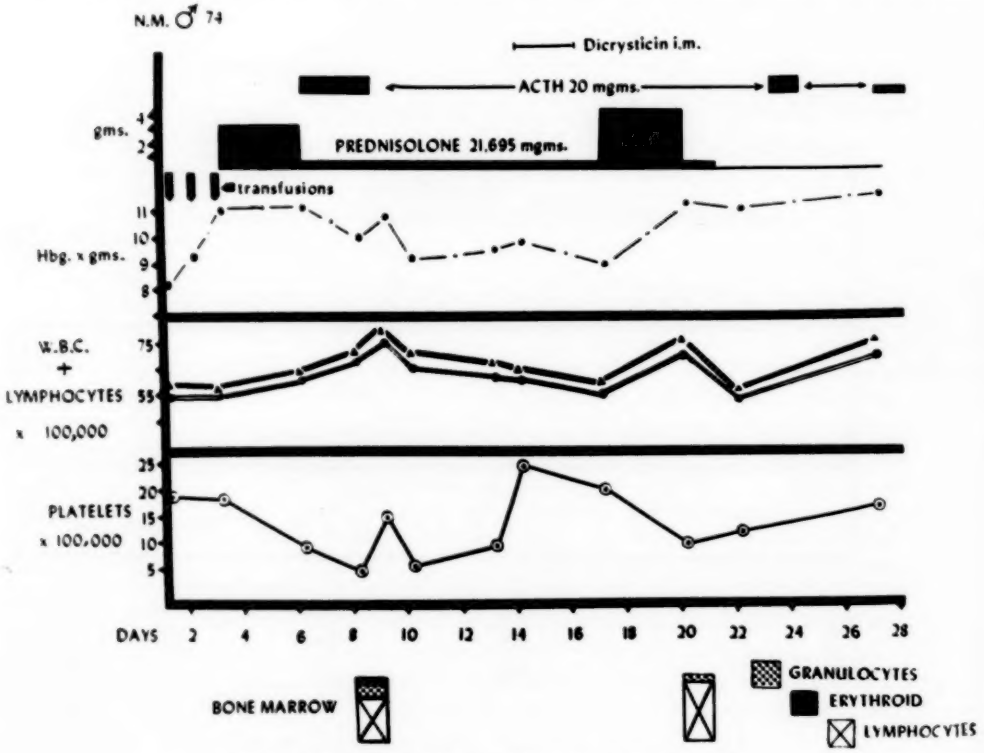

FIG. 4. Case 13. Chronic lymphocytic leukemia.

centage of lymphocytes; the platelet count had fallen to 50,000. A bone marrow smear on this date exhibited hypoplasia, with 81 per cent lymphocytes. On the twenty-first day, after a total of 21,890 mg., prednisolone was discontinued. The nodes had decreased to approximately 20 per cent of their original size. The following day the patient received 6 mc. of H_3PO_4-P^{32}, and one month later 3 mc. of $CrPO_4$-P^{32} was injected directly into the lymph nodes. The leukocyte count decreased to 99,000 with 96 per cent lymphocytes. During prednisolone therapy there was no significant increase in the levels of blood sugar, sodium or potassium. The patient maintained a sense of well being.

In this patient, there was rapid reduction in the size of the lymph nodes with disintegration of leukemic cells, but no significant reduction in the leukocyte count. Platelets were slightly depressed after maximum dosages of prednisolone. It is believed that more prolonged dosage would have ultimately induced a fall in the leukocyte count, as in other cases.

In Figure 5 is a summary of our experience with massive dosages of prednisone and prednisolone in acute leukemia (excluding subacute cases and chronic cases which became acute). Of a total of 23 patients treated, 10 were over the age of 30 years. Of the 6 remissions occurring in adults, 3 were considered complete; each was distributed in a different category, according to cell type. In 6 of the patients over 30 years of age, prednisone or prednisolone was the first and only specific antileukemic therapy; 3 of the 6 obtained remissions (1 partial and 2 complete).

Table 2 shows a classification and analysis of side effects observed during and shortly after treatment with these steroids.

TYPE OF LEUKEMIA	FAILURE	PARTIAL REMISSION	COMPLETE REMISSION	TOTALS
Acute Granulocytic	A.N. ♂ 35 ✱† C.G. ♂ 69 E.R. ♂ 41 ✱†	F. H. ♂ 47 ✱ J.S. ♂ 17 E.G. ♀ 22 ✱† E.B. ♂ 51	T. R. ♂ 62 R.S. ♂ 8	10
Acute Lymphocytic	K.L. ♀ 4½ J.M. ♀ 20 S.H. ♂ 30 ✱†	J.E. ♂ 4½	J.G. ♂ 12 ✱† K.B. ♀ 3 J.M. ♂ 12 C.H. ♂ 6½ ✱ E.R. ♂ 26 ✱† M.G. ♂ 11 M. E. ♂ 8 N.M. ♀ 51	11
Acute Monocytic		M. H. ♀ 81 ✱†	A.H. ♀ 34	2
TOTALS	6	6	11	23

✱ Leukemia previously not treated. † Steroid only specific chemotherapy.

FIG. 5. Summary of experience with massive dosage of prednisone or prednisolone in acute leukemia.

TABLE 2

Side Effects

Name, Age, Sex	Abnormal		Blood Sugar (mg./100 cc.)		Blood Pressure Rise				Psychosis, Depression, Euphoria	Wt. Gain over 5 lbs.	Excessive Weakness or Low B. P. on Withdrawal
					Systolic		Diastolic				
	K	Na	120–160	Over 160	10–20	over 20	5–10	over 10			
N. M., 51, F.....		L*		Yes		Yes		Yes	Yes		
M. H., 81, F.....	H		Yes								Yes
T. R., 62, M.....				Yes						—	Yes
S. H., 30, M.....				Yes					—		—
E. B., 52, M.....	L		Yes						Yes		—
F. H., 47, M.....				Yes							
C. H., 44, M.....	—	—	—	—	—	—	—	—		Yes	
A. N., 35, M.....	H			Yes							
O. S., 46, M.....			Yes		—	—	—	—		Yes	
R. H., 44, M.....	H			Yes						Yes	
O. H., 34, F.....	—	—	—	—							
N. M., 74, M.....						Yes		Yes		Yes	
B. S., 53, F.....	—	—	—	—	Yes			Yes		Yes	Yes
E. R., 41, M.....		L				Yes		Yes			
T. S., 72, M.....			—	—							
C. V., 56, M.....										Yes	
C. G., 70, M.....				Yes						—	
Total.....	4	2	3	7	1	3	0	4	2	6	3

* L = Below normal range.
H = Above normal range.
— = Not determined.
Blank space = Normal values.

DISCUSSION

Although survival time is the ultimate criterion of our overall care of the leukemic patient, the remission rate, of necessity, must be used to assess the value of individual agents. The standards set for remissions vary with each author. Because of the great difference in effect of the various antileukemic agents on the various formed elements of the blood, complex and rigid criteria of remission are not altogether satisfactory. In this study, mere clinical remissions were not accepted; in addition, there had to be definite and sustained improvement in laboratory findings. In order of approximate importance, the following factors were considered: reduction of blast forms in the bone marrow, decrease of blasts in the peripheral blood, decrease in the leukocyte count if elevated, increase in the platelet and erythrocyte counts, and an increase in the hemoglobin level. A definite break-point in the number of blast cells was observed in every remission, with a significant and sustained drop to much lower levels or to zero. Remissions were considered complete when blood counts were normal and the proportion of blasts in the bone marrow was less than 10 per cent. Moreover, the remission had to be maintained for at least two weeks.

This series demonstrates that some cases of acute leukemia in the adult can

be treated beneficially with massive dosage of prednisone or prednisolone. Of particular interest was the favorable response of the 2 cases of monocytic leukemia, ordinarily regarded as refractory to treatment, especially with hormones (7). More important, perhaps, is the fact that acute granulocytic leukemia, the most frequent form of the acute disease in adults, may respond favorably. The rapidity of response to massive therapy is remarkable. Blasts may be cleared from the blood in a few days and from the marrow in well under two weeks.

Adverse or side effects do not appear to increase in proportion to the dosage. No serious abnormalities of blood potassium or sodium levels were observed. It was found best not to give potassium routinely at the beginning of therapy, since levels above normal were observed in 2 cases following administration of 1 to 3 grams of potassium chloride daily by mouth. Some patients were given low-salt diets, and in 2 of these the blood sodium level dropped below normal. Elevation of blood sugar concentration was the most common side effect, but in no case did it reach as high a value as 200 mg. per 100 cc.; there were no adverse clinical effects, and in each case the level subsided to normal on discontinuing the drug following the desired hematologic response. Elevation of blood pressure was noted in 4 cases; it was not severe and was not considered an indication for withdrawal in any instance. One patient exhibited transient mental confusion and depression, which cleared at the end of therapy. In another a definite psychosis developed, and became worse immediately after withdrawal of medication; after subsequent marked improvement, there was a relapse requiring psychiatric care and convulsant therapy. The psychiatrist expressed the opinion that a psychosis would have developed in this patient sooner or later without prednisone.

Proneness to severe infection was not included in side effects, because leukemic patients are definitely prone to infection, without treatment, and it was therefore impossible to determine the effect of steroid therapy alone. Nevertheless, massive dosage with these drugs was considered as a calculated risk and antibiotics were employed in a manner considered most likely to reduce this risk. In the acutely ill leukemic patient, the two greatest risks are death from infection and death from hemorrhage. If such a case is amenable to massive steroid therapy, the effect on the leukemia will immediately reduce these risks. Combined with antibiotics, the result may be dramatic When a case is not responsive to steroid therapy, the increased risk may be largely neutralized by the use of antibiotics and substitution of combined antimetabolite therapy.

The possibility of approaching toxic doses when using amounts in the range of 3 to 5 grams daily should be considered. In some cases a drop in the platelet count is associated with maximum steroid dosage; in others it occurs slightly later in the withdrawal phase. The bone marrow may become hypoplastic for a while, but following its recovery the platelet count may rise to normal and a complete or nearly complete remission may be obtained. This is exactly what happens during administration of the slower-acting antimetabolites. As in the case of these latter drugs, it may prove necessary to use steroids such as prednisone and prednisolone in nearly toxic dosage in order to obtain a response in

the maximum number of cases of acute leukemia in adults. For most patients 1 gram daily should suffice; a few may require up to 3 grams daily. Larger doses up to 5 grams should be employed with great caution and with frequent study of the bone marrow and blood chemistry. Weakness following withdrawal of the drug can be prevented by a tapering-off process, sometimes combined with the addition of ACTH therapy. In the aged, this process may have to be more prolonged.

SUMMARY AND CONCLUSIONS

Remissions have been obtained in acute granulocytic, lymphocytic and monocytic leukemia in patients over the age of 30 years, as well as in younger groups, with massive doses of prednisone and prednisolone. Dosages up to 5 grams daily (100 times the ordinary therapeutic range) have been used with benefit. Massive therapy seems indicated in 1) the acutely ill patient who cannot wait for the effects of antimetabolic therapy, 2) the patient who is apparently unable to achieve a satisfactory remission after adequate and prolonged antimetabolic therapy, and 3) the terminal case, in which all other possibilities and combinations of therapy have been exhausted. In such instances, it is possible to obtain one more, and sometimes a surprisingly good remission, thus prolonging survival time. Viewed against the background of experience with 121 cases of acute leukemia analyzed for a recent five-year period, we believe that the use of massive steroid therapy, alone or in combination with other available antileukemic agents, will lengthen survival time.

REFERENCES

1. Bross, I. D. J.: Statistical analysis of clinical results from 6-mercaptopurine, *Ann. New York Acad. Sc.* **60:** 369–373, 1954.
2. Stickney, J. M.: *in* Proceedings of the Second Conference on Folic Acid Antagonists in the Treatment of Leukemia, *Blood* (Suppl.) **7:** 115, 1952.
3. Burchenal, J. H.: *in* Proceedings of the Second Conference on Folic Acid Antagonists in the Treatment of Leukemia, *Blood* (Suppl.) **7:** 116, 1952.
4. Scott, R. B.: The treatment of acute leukemia, *Brit. M. J.* **2:** 75–77, 1955.
5. Haut, A.; Altman, J. S.; Cartwright, G. E., and Wintrobe, M. M.: The influence of chemotherapy on survival in acute leukemia, *Blood* **10:** 875–895, 1955.
6. Third Report to the Medical Research Council by the Panel on the Hematological Applications of ACTH and Cortisone, *Brit. M. J.* **2:** 455–457, 1955.
7. Wintrobe, M. M.; Cartwright, G. E.; Fessas, P.; Haut, A., and Altman, S. J.: Chemotherapy of leukemia, Hodgkin's disease and related disorders, *Ann. Int. Med.* **41:** 447–464, 1954.
8. Hayhoe, F. G. J., and Whitby, L.: The management of acute leukemia in adults, *Brit. J. Haemat.* **1:** 1, 1955.
9. Bernard, J., and Deltour, G.: Les nouveaux traitements des leucoses; T.E.P.A.—G.T.41 (myleran)—6-mercaptopurine—β-mercaptoéthylamine; doses très fortes de cortisone, *Semaine hôp. Paris* **29:** 3430–3436, 1953.
10. Hill, J. M., and Vincent, L.: Traitement des leucémies aigues par la fluorohydrocortisone, *Sang* (Paris) **26:** 269–281, 1955.
11. Hill, J. M.; Speer, R. J.; Falco, D.; Marshall, G. J., and Smith, A. L.: Scientific Exhibit at the Annual Meeting of the American Medical Association, Atlantic City, N. J., 1955.

DISCUSSION

Chairman McGavack: This paper is now open for discussion.

Dr. Ellison (Memorial Hospital, New York City): With regard to Dr. Hill's paper, we have treated 5 patients over the age of 30 years with acute leukemia, using dosages of 1 gram of Meticorten daily. Our results have not been as good as those reported, but we obtained a complete remission in one man 43 years of age. We have been a bit more wary of side effects, because 1 patient had an acute perforation of the sigmoid colon with masking of the acute abdominal symptoms. In 1 patient a duodenal ulcer of thirty years' duration was reactivated.

One patient with chronic lymphatic leukemia showed marked improvement with Meticorten; the liver and spleen decreased in size. We have not had favorable results in chronic myelocytic leukemia in an acute phase. Similar to Dr. Hill's experience, hyperglycemia developed in almost all of these patients, but not to a degree to cause difficulty clinically. There was no elevation of blood pressure in any of the patients so treated.

Chairman McGavack: Any comment, Dr. Hill?

Dr. Hill: Only that I was interested in the acute perforation. We have been looking for that and have not had it in any of our patients. In a patient who died and in whom therapy had failed, there was some superficial ulceration of the gastric mucosa. We almost routinely administer antacids, which may be of some help.

We deliberately used a massive dosage in 1 patient with a history of ulcer, who had had bleeding on several occasions. Upon the advice of the internist, the dosage of aluminum hydroxide gel was doubled. The patient had no difficulty during this phase of the treatment.

One patient did not, and another did, have an activation of pulmonary tuberculosis. This occurred after a remission, and we were puzzled by his fever.

I should like to make one other comment.

Somewhere around a dosage of 3 to 5 grams daily we may be approaching—and I say this with caution—the toxic level. With such heavy dosage, it may be that there is some tendency toward depression of the bone marrow. If so, that would not be unlike the action of other successful antileukemic agents, and perhaps like that of the antimetabolites. In order to get the greatest number of remissions, and the last possible remission, this drug may have to be pushed, as the antimetabolites have to be pushed, close to a toxic level.

I hesitate to use the word "toxic," because I believe there is no abrupt toxicity as with the antimetabolites, but I know no other word to use. It may be that we have approached the practical limits of dosage.

PROBLEMS OF GERIATRIC CARE*

JOSEPH H. SHELDON, C.B.E., M.D., F.R.C.P.

The Royal Hospital, Wolverhampton, and the University of Birmingham, School of Medicine, England

Because intense concern with geriatrics and gerontology is of recent origin, I shall try to give the relevant background before dealing with problems of geriatric care.

The problems of old age have really burst upon a startled world since the end of World War II. They have achieved such prominence in some countries as to lead to the foundation in 1950 of an international association for their study, the International Association of Gerontology. Although the International Association itself is only five years old, this is not because there have never been old people in the world. I do not say that vital statistics of Methuselah's time would be acceptable now, but there were old people, though never enough to affect the state of civilization. It appears, in general, that in a partly industrial and partly rural civilization, like this country or like Europe, the strains on the community become sufficiently severe to make themselves felt when the population over 65 years of age reaches 7 to 8 per cent.

The change in population structure is due to the simultaneous operation of two distinct processes. The first is the general emancipation of women, which, coupled with the techniques of birth control, led to a lowering of the birth rates. Its importance is shown by the fact that in 1950 Great Britain's birth rate was only about one third of what it was in 1870. An ordinary population chart suggests a pyramid, with the maximum number of individuals occurring in the first five years. The numbers gradually decrease with the years, owing to the operation of the natural processes of loss by famine, pestilence, disease, and so forth until finally there are a few survivors in the eighties and nineties at the top. A lowering of the birth rate means that the lower tier of the pyramid may, for the first time in history, become less than the part immediately above it. What is known popularly and correctly as the bulge in the pyramid is the first process. Since the bulge takes sixty-five years to reach the beginning of the old-age period, in 1955 the population is affected by the birth rates of the 1880's and 1890's.

The second factor is that the increased control over death rates, particularly over mortality from infection in the early years of life, will result in the bulge being larger than would formerly have been expected. Therefore a large number of people who normally would have died earlier are now reaching the old-age period, while at the same time there are fewer in the younger generation to look after them. One effect of this in Great Britain is that an estimated 25 per cent of the old people have no children attached to them. This is a fact of tremendous social importance.

* Address presented at Veterans Administration Hospital, Houston, Texas, May 2, 1955.

In Great Britain, the population of those over 65 years of age remained steady at 5 per cent throughout the last century and up to the 1911 census. In 1921, it began to climb and reached 6 per cent; in 1931, it was 7 per cent; in 1951, it had gone up to 11 per cent; it is now probably near 12 per cent. By 1971, old people are likely to account for 16 to 19 per cent of the total population. The present population of 5 million old people is going up to a population of perhaps 7.5 or 8 million. The percentage of old people in the United States is rising in the same way. The problem today is nowhere near as severe as it is going to be.

Still another process is affecting the older population. Of all elderly people aged 65 years or older in 1931, 43 per cent were between the ages of 65 and 70 years and 57 per cent over age 70. Following the advent of antibiotics and with the consequent saving of lives, more people remained alive past the age of 70 years. By 1951, 62 per cent of elderly people 65 years or older were past 70 years of age, while the proportion of those 65 to 70 years of age had changed to 38 per cent. The reduction attributable to antibiotics of mortality from pneumonia and infections has also affected the ratio of men to women. There are now relatively many more women than men alive in old age, because women have the longer life expectancy, though they do not live as healthily. This means that we are probably faced with a bigger problem in medical and social care.

In terms of actual practice, these changes in the population structure mean that a great strain is thrown on all community organizations concerned with the care of old people, whether the problems be medical, psychological, or social. These three aspects complement and affect one another, and cannot be separated when old age is dealt with on the community level.

WHEN OLD AGE BEGINS

When *does* old age begin? Old age officially begins in Great Britain at 65 years for men and 60 years for women. The beginning of real aging can be defined as that time when an individual loses the ability to be completely independent of others in just simple living. One of the extraordinary things about old age is its amazing variation; some people start to age and are finished in their forties or fifties, whereas others are still alive physically and mentally in their nineties. The causes for that individual difference urgently need investigation. Nobody has any clear idea of what they are. There is little doubt that to some extent aging is a genetic phenomenon, and factors such as the maintenance of an active mental life and a feeling of usefulness have some bearing.

Examination of certain activities of people in a community can supply definite information on the average onset of old age as defined in terms of biological independence. The following figures are from a survey of the population of my own town, Wolverhampton, which I made some years ago. The extent to which women were able to take sole charge of their households and homes was investigated, with these findings: at 60 to 70 years of age, 50 per cent of the women had entire charge; at 75 years, the percentage was 40; at 80 years, the percentage was 18, and at 85 years of age, 4 per cent of the women still had entire care of

their households. Women do not retire from the drudgery involved in such work; they continue for as long as they can, because they have the deep satisfaction of knowing that they are necessary to other people. The figures suggest that between the ages of 70 and 75 the increase in effects of age forced these people to give up. The longer an old person lives in a community, the greater is the possibility that accidents of life will befall his children and subject him to greater strain, such as that involved in caring for grandchildren. After 70 years of age, the number of old people capable of meeting the strain steadily decreases.

Another type of movement is specific for old age: movement limited to the house. This type of limited movement makes a difficult situation for relatives, for though it may be due partly to physical weakness in the old person it also may be due to mental conditions. The proportion so affected begins to rise after 70 years of age, indicating that aging begins between 70 and 75.

MAINTENANCE OF GOOD HEALTH

The following discussion will deal with the period beyond 75 years of age. The people in this group were found in the survey to fall into various categories of mobility. Two per cent were bedridden at home; 10 per cent could only move about the house; 66 per cent were still able to get about as much as they liked. The remaining 22 per cent could get outside but were limited in movement by various physical defects. It is particularly important to look after this last group, for proper treatment may prevent these people from falling into the "house only" or the bedridden class.

Consideration of the main physical aspects of aging about which something can be done leads to the conclusion that attention should first be given to maintenance of good health rather than to treatment of disease. When old people are in good health, they can be of service to the community. Several specific problems need attention.

Old people suffer greatly from defects in the organs of perception, the eyes and the ears, because old age is a time of life when the body requires all the information that it can get. Sixty-five per cent of all old people at the age of 85 suffer from deafness due to a decline in the hearing of high tones, and 95 per cent or more of old people at that age require spectacles for close work. Whenever a community must make certain that its old people are in the maximum state of useful health, those are the two things to look for first.

The teeth tend to wear out in old age. There is some doubt, however, concerning the desirability of supplying dentures to old people. Dentures require a little adaptation, and very few old people given them for the first time will admit that they fit. Several old people were found to accept the dentures but not to wear them at home. In fact, about 14 per cent of the elderly individuals in the survey used their dentures only for cosmetic and social reasons, not for eating. The reason is that in old people it is natural to eat on the gums. An amazing amount can be done with the gums, given time and practice; and when old people are used to eating on their gums, it seems advisable to leave them

alone. People who are going to need dentures should have them earlier in life, so that they can become accustomed to them.

A highly important factor in the health of old people is care of the feet, as painful feet cause considerable disability in the old-age population. The men were found to have a maximum incidence of pain in the feet in the seventies, which may be due to a spreading of the ligaments, but women were found to have a steady incidence of about 40 per cent through the whole old-age period. The most frequent cause of the limitation of movement that hampers 22 per cent of the old-age population was found to be cardiovascular disease. The second most frequent cause was arthritis, the third was respiratory disease, but the fourth was pain in the feet. The high incidence of painful feet is a major challenge to preventive medicine, and much of this pain is preventable.

Among many kinds of foot trouble, old people suffer from long, uncut nails and from a tremendous number of corns and callosities. Often they cannot bend over or see well enough to cut their own nails. The relief they obtain from proper care of the feet is astonishing, and it makes a great difference in their domestic efficiency. Another cause of painful feet is deformities of the foot, such as hallux valgus and bunions. These conditions are probably due to the wearing of tight shoes and socks early in life. When the population of elderly people reaches 18 or perhaps 20 per cent of the whole, care of the feet for that group will be as essential as it is for an army. Neglect results in a great loss of efficiency.

ASPECTS OF AGING THAT NEED INVESTIGATION

Three principal difficulties complicate the problem of maintaining the health of old people. The first is that attached to the diagnosis of physical illness. The theory of the single diagnosis, which is usually acceptable when dealing with younger people, does not apply to old people. As many hypotheses as are necessary to fit the physical signs may be made. A large number of postmortem examinations have shown how frequently there are multiple pathological changes with two or three conditions present at the same time.

Another complication is that the clinical picture of disease in the aged is different from textbook descriptions, which mainly apply to younger people. Obvious differences are that elderly people do not react to stress in the same way as younger people and do not exhibit the same temperature reaction to infection. Frequently, old people experience less pain from things like coronary thrombosis.

The third important difficulty is that many things remain entirely unsuspected because of the length of time they have existed. A woman with nutritional anemia and a hemoglobin level of 50 per cent may be unaware of her illness simply because it developed so gradually. The slow growth of a carcinoma may arouse no concern. This sort of thing, coupled with the possibility of multiple diagnosis, makes the care of old people difficult. The particular problems encountered with old people make adequate clinical examination highly important. These difficulties offer tremendous scope for discovery and research.

There are several highly important aspects of aging on which very little work has been carried out. Among these is a decline in postural control, which can result in falls with serious consequences. Old people fall in one of four ways: in an attack of vertigo, by tripping, by adopting certain positions, or by their legs giving way. They fall because too much strain is put on their balancing mechanism. Curiously, the strain on their balancing mechanism that affects them most is working with their heads thrown back, as in reaching for the top shelf of the larder or trying to replace an electric light bulb. If the top shelf of the larder were put out of bounds for everybody over 70 years of age, many casualties would never occur. Old people themselves always say the same thing about falling by tripping or by losing their balance: that once they start to go, they know they can do nothing about it. This is surely a problem for physiology, for it means that the involved nervous circuits (so to speak) in the brain are so active as to be occupied by consciousness, yet at the same time have such a defect that they cannot take control.

The most interesting group of falls is that in which an old person says his legs give way. These sudden falls are quite different from tripping. Old people who fall this way cannot be simply picked up and put in a chair, for they are completely powerless. This type of fall resembles an attack of cataplexy in younger life. It seems to be due to a decline in function of the postural mechanisms whereby an interruption in the stream of impulses necessary to maintain posture occurs, resulting in an abrupt fall. This is a subject worth studying.

A difficulty similar to that involved in tripping and losing of balance is encountered by the old person trying to cross the street. There is a slowing up in the "timing mechanism," and though the old person looks up and down the street, and his mechanism scans the location, the angle of approach, and the speed of oncoming vehicles, by the time the predictor mechanism in his brain has decided whether or not it is safe to cross the road the situation has changed. In many cases very old people seem to get a sort of retroactive inhibition and may cross the road only when the lights are wrong. This is not due to just muddle-headedness or obstinacy, but to a malfunction of the timing mechanism.

One of the most characteristic of old-age physical phenomena is difficulty in the dark. By the age of 80, about 90 per cent of women found it hard to get around in the war-time blackout. This kind of difficulty seems to be due to the increasing dominance of the eyes in old age and the increasing decline in importance of proprioceptive sensation.

There are also problems concerning the mental aspects of old age which need to be investigated. One that is too often overlooked is that we know nothing about old age as an old person experiences it. A great deal could be learned from old people with sufficient education and intelligence to describe what it is like to be old.

One thing younger people fail to understand is the intermittency of old age. At ten o'clock in the morning a person 80 years of age might feel 40, at eleven o'clock he might feel 80, and at twelve o'clock he might feel 40 or 50 again. This is a characteristic of declining function.

SOCIAL IMPLICATIONS OF AGING

Those who have much to do with old people realize the tremendous importance to them of their physical possessions, such as collections of letters and other things, their spectacles, and their teeth—all those things that in old age become extensions of the personality. When old persons must be taken into an institution, it is fatally easy to take them away from their environment and those physical contacts, and so to depersonalize them.

One of the worst things in old age is the feeling of uselessness, which hurts old people more than anything else. Two things essential to maintenance of the mental health of old people are, 1) to give them a sense of use in the world, and 2) to overcome their sense of loneliness.

Loneliness is one of the most serious social effects of aging. Eight per cent of old people were found to be definitely lonely and about 25 per cent were somewhat lonely. In all these cases there was a decline in both physical and mental vigor. The relief of the very lonely, an aspect of social structure of great practical importance, can only be achieved by a combination of voluntary and other efforts. In Great Britain, clubs and visiting agencies assist in this work, and there will be even more need for such services as the proportion of old people in the community increases.

The main social implication of aging is making the proper use of hospital beds, because unless that be done the community cannot carry the load. In Great Britain, about 95 per cent of the old people are living at home by themselves, or they are living with their families or their children. When they become ill and have to enter the hospital, the social structure is disrupted. A big problem is that of the isolated old people who live alone. When anything happens to them, they have to be treated in an institution. When they are better, they cannot always be sent out, because there is no one to look after them at home. A liaison between the hospital and the home services, whereby some home care after discharge is provided, is a solution being developed in Great Britain.

As the proportion of old people in the community rises, there is increasing need for the integration of the domestic and the social care of aging. About 8 per cent of old people are a tremendous burden to their families. Hospitals, by cooperating with the families, can help relieve the strain and make it possible for the family still to carry the burden.

Various schemes have been tried. One hospital developed a system of bringing the relatives in and teaching them the home nursing care required in the particular case. Families always responded when their help was enlisted and they were given an honorable place as partners in the care of the old people. Another experiment was to take an old person in again when the family needed a holiday. Through methods such as these, the community must face the increasing burden of caring for old people.

These problems are indicative of a vast untapped field of work in clinical medicine. Your institution has wonderful possibilities of developing and integrating research in gerontology and in geriatric care. It is of tremendous importance that such centers, with research as well as clinical facilities, should attack these problems, which are as important as they are interesting.

MANAGEMENT OF FOOT LESIONS IN THE ELDERLY DIABETIC*

DAVID HURWITZ, M.D.†

Harvard Medical School and the Boston City Hospital, Boston, and the Mount Auburn Hospital, Cambridge, Massachusetts

In a recent paper we have urged a conservative approach to the management of foot lesions in the diabetic (1). Because diabetes is common among elderly patients and because diabetes accelerates the aging process, knowledge of the management of these lesions is of importance to those dealing with geriatric problems.

Diabetes of long standing is commonly associated with coronary artery disease, retinopathy, nephropathy, and peripheral vascular disease. Among elderly diabetics, peripheral vascular disease is one of the leading causes of hospitalization. Formerly these patients were subjected to early high amputation as a life-saving measure and thereafter remained severely disabled and restricted to a chair-and-bed existence, since they were not physically or mentally competent to learn how to use a prosthesis. During recent years there has been a growing realization that conservative management of foot lesions, particularly of infections, is often rewarded by successful preservation of intact feet and legs. Such an approach requires weeks or months of hospitalization with its attendant expense, but it is thoroughly worth while if the patient is able to leave the hospital walking on his own two feet. Major amputations may require only two or three weeks of hospitalization, but the patient is left a demoralized, dependent person representing a burden to his family, his community, and himself. The purpose of this paper is to discuss some of our experiences and observations in the management of foot lesions at the Boston City Hospital in the past five years.

PREVENTION

An important aspect of this problem is prevention of infections of the feet. Good foot hygiene would prevent many serious infections. There should be daily washing of the feet, with special emphasis on cleanliness between the toes and treatment of epidermophytosis. Instruction in foot hygiene is an important part of the general instructions to the new diabetic. Patients are told to report immediately if they note any area of redness, ulceration, or discoloration. Such changes are considered to be serious and usually necessitate hospitalization. Heat, strong chemicals, and pressure from new shoes must be avoided. Patients

* Some of the data presented in this paper previously appeared in an article by the author in the March–April 1955 issue of *Diabetes* (1). Permission to include these data has been kindly granted by Dr. Franklin B. Peck, Sr., Secretary of the American Diabetes Association.

† Chief of Diabetes Service, Boston City Hospital; Chief of Division of Medicine, Mount Auburn Hospital; and Assistant Clinical Professor of Medicine, Harvard Medical School.

with foot lesions constitute a large percentage of admissions for diabetics, as we practically never admit new patients from the Out-Patient Department at the Boston City Hospital for regulation, preferring to manage them on an ambulatory basis. Thus, about two-thirds of all hospitalized diabetics at the Boston City Hospital are admitted for treatment of foot lesions.

INFECTIONS

Infections in the feet of diabetics are often secondary to epidermophytosis or other skin infections—usually in feet with some impairment of the circulation. It is important to differentiate infection from gangrene. Confusion occurs when there is a great deal of slough which might be mistaken for gangrene. It is our feeling that these patients should be followed closely by both the surgeon and the internist, and that the role of the internist should be to regulate the diabetes and to urge the surgeon to disregard the diabetes in dealing with the infections of the feet. Too often surgeons are reluctant to cut into infected areas in the feet in the presence of diabetes; and they will often tolerate pus under pressure in the diabetic, whereas they would never allow it in the nondiabetic. Wide local incision should be performed early and repeated as often as necessary to insure removal of slough and provide adequate drainage. It is important that the foot be inspected daily to make sure that there is no pocketing of pus. Sometimes four or five trips to the operating room may be necessary before all pockets are adequately drained. Osteomyelitic metatarsals should be removed or resected. Sometimes the area of drainage is so large and wide that one wonders whether healing to the point of a useful foot can ever occur without plastic surgery. However, if all the slough is removed and the wound shows clean granulation, it is often surprising how rapidly healing may take place without the necessity of skin grafting. One should not be discouraged if there is no dorsalis pulse in the presence of infection and edema, because the pulsation often returns after the subsidence of the edema. The following is an outline of our plan of treatment:

1. All patients, including those with even minor foot infections, are hospitalized. They are given a complete physical examination to detect other complications commonly found in diabetics of long standing.

2. An adequate diet, as high as possible in proteins, is ordered. This is important, since the nutritional state of these patients is often poor and, even if the diabetes is well controlled, good healing does not take place unless caloric and total nutritional needs are met.

3. Diabetes is brought under good control. These patients often require much more than their usual dosage of insulin when infection is present. We attempt to get the urine as close to sugar-free as possible, without causing hypoglycemia.

4. Cultures are made of material from the infected areas and sensitivity studies are carried out; then appropriate antibiotics are given. If no open lesion is present, penicillin should be given in doses of 600,000 to 1,000,000 units daily.

5. Wide drainage of the infected area should be undertaken within twenty-four hours of admission, and repeated according to need thereafter.

If the foregoing plan is carried out, high amputation is rarely necessary for infections of the foot. Our rule is that high amputation should not be performed unless there has been a two-week period of conservative treatment; by that time it is rarely necessary.

GANGRENE

The same good outlook is not present with true gangrene. It is important to differentiate true gangrene from necrotic slough due to infection, since the latter carries a better prognosis. Removal of a toe or a transmetatarsal amputation may be adequate in some cases of true gangrene, but many more require higher amputation. Recently we have successfully recommended below-the-knee amputation in cases with good popliteal pulses. This should be tried mainly in patients who are candidates for prosthesis. The value of sympathectomy is doubtful in these cases; often it is carried out because there is nothing else to offer. Recent critical studies by surgical clinics confirm this impression (2). Berry, Flotte and Coller (3) state that there is a minimum chance of obtaining a good result from lumbar sympathectomy when the following conditions exist:

1. Elderly diabetics (over 65) with clinical evidence of arteriosclerotic involvement of other organs or elevated systolic blood pressure.
2. Severe atrophy of the soft parts of the leg with evidence of marked capillary anoxia.
3. Severe pain in the foot or lower third of the leg, and no popliteal pulses.
4. A rapidly progressing process with widespread arterial involvement.
5. Gangrene or ulceration of the foot in patients over 60, with severe pain and obliteration of popliteal pulses.

Since at least two of the foregoing conditions usually exist in our patients, sympathectomy has little to offer. We do not recommend this procedure routinely in foot lesions associated with diabetic arteriosclerotic disease. Several of the patients discussed subsequently underwent sympathectomy, but it did not appear to alter the progress of the disease.

The following cases are illustrative:

Case 1. Mrs. McI., a 60-year-old woman, was admitted to the Boston City Hospital because of an infection occurring after her foot had been stepped on two weeks previously. For about a month she had had symptoms of polydipsia, polyuria, and a 15-pound weight loss. She had never been told that she had diabetes.

A large area of fluctuation near the heads of the first and second metatarsals was found on the dorsum of the foot. All the toes were cyanotic. No dorsalis pedis or posterior tibial pulses could be felt, but both popliteal arteries were palpable.

The diabetes was readily controlled with 30 units of NPH insulin. The patient was advised by the Surgical Service to have a mid-thigh amputation, but she refused. Penicillin therapy was started, local drainage was begun, and wet soaks were applied. The second toe and distal phalanx of the great toe were amputated. The wound on the dorsum was closed by a skin graft, with a 95 per cent take. The patient walked out of the hospital three months after admission.

Case 2. Mrs. W., a 59-year-old Negress, had diabetes three years before this hospital admission, controlled by 20 units of insulin. Her chief complaint was swelling of the left foot caused by slamming a door on it three days previously.

There was marked swelling of the entire foot, with a hematoma on the dorsum, and the second toe was black. There were no dorsalis pedal and posterior tibial pulses. The popliteal pulse was bounding.

The diabetes was regulated with 85 units of insulin daily. Penicillin therapy was started. A left lumbar sympathectomy was performed. The foot was debrided, and the second toe was amputated. The dorsum of the foot was skin-grafted, with a good result. Complete healing occurred, and the patient was discharged ten weeks after admission.

Case 3. Mr. R., a 56-year-old man, was found to have diabetes seven years previously, during an appendectomy. He had been advised to take 10 units of protamine zinc insulin daily but had discontinued it when the results of urine tests for sugar were negative. Six years before admission he was hospitalized for diabetes (with no complications) and was again discharged on 10 units of protamine zinc insulin. Six days before the present hospital admission he had pared a corn on the fifth toe with a razor blade; following this the toe became painful and swollen and began to drain.

The fifth toe was swollen, red, tender, and was oozing pus; the entire foot was swollen, hot and tender. The dorsalis pedal and posterior tibial pulses were not palpable. The diabetes was controlled with 35 units of protamine zinc insulin and 20 units of regular insulin. Penicillin therapy was started, and the fifth toe was debrided and dressed with wet packs. The cellulitis subsided gradually. A right lumbar sympathectomy was performed. The patient was discharged after two weeks of hospitalization. Two weeks later he returned because the fifth toe on the same foot was reinfected, necessitating its amputation. The infection had spread between the fascial planes. The dorsal and plantar surfaces of the foot were incised, necrotic tissue was removed, and the wounds were kept open. Subsequently, the wounds healed well, and the patient was discharged after three months of hospitalization.

Case 4. Mrs. P., a 72-year-old widow, was admitted because of a sore left foot. She had diabetes of eighteen years' duration and was treated with 40 units of NPH insulin. Three years before, she had trimmed a callus of the right foot, with resultant cellulitis and gangrene; a mid-thigh amputation had been performed. One month before the present admission, blisters developed on the left foot as a result of ill-fitting shoes.

Physical examination showed that the second and third toes on the left foot were black and dry, with redness of the surrounding tissues. No pedal or popliteal pulses were felt. A left sympathectomy was performed on October 15, 1952. The second and third toes were amputated on November 5. The wound healed well, and the patient was discharged on December 14, after two months of hospitalization.

Case 5. Mrs. C., a 69-year-old woman, was admitted because of marked dyspnea. She had diabetes of six years' duration and had been taking 10 units of protamine zinc insulin daily. Two weeks previous to admission she noticed a "water blister" on the left toe, which she treated with potassium permanganate soaks and some type of powder.

On physical examination the temperature was 101°F., the pulse 130, and the blood pressure 180/108. There were rales at both lung bases, an enlarged heart, and a grade II apical systolic murmur. The left great toe was swollen, dark, and necrotic. The second and third toes were fissured and black with seropurulent discharge. The bone of the second toe was visible. There were no pedal pulses. The diabetes was controlled with 10 units of NPH insulin daily. The cardiac failure was controlled with digitalis therapy. The second toe and metatarsal head and the distal phalanx of the first toe were excised. An incision was made along the entire plantar aspect of the foot for drainage. Saline soaks were administered. Slow healing took place, and the patient was discharged November 19, 1952. She was readmitted on December 10 with osteomyelitis of the remaining portion of the first

toe, which cleared following ten days of penicillin therapy. She was discharged after three and a half months of hospitalization. The patient is limited by her cardiac status, but has a functional foot.

Case 6. Mrs. K., a 72-year-old woman, was admitted to the Boston City Hospital on December 21, 1954 because of an ulcer on her left foot. She had had an old thrombophlebitis with lymphangitis for some years. Diabetes had been known for three years.

On examination there was edema and thickening of the skin of the entire left leg, consistent with an old phlebitis. On the bottom of the foot there was an ulcer with pus draining from it. The plantar surface of the foot was markedly swollen.

During her hospital stay she was well maintained on 20 to 30 units of NPH insulin. The plantar surface of the foot was incised and drained but progress was poor, so that on February 26, 1955, two months after admission, a supracondylar amputation was advised after consultation at Grand Rounds with the senior surgeons. At this point we urged further wide drainage, which was carried out on March 25, 1955. Two longitudinal incisions were made on the plantar surface of the foot, following which there was drainage of purulent material. The foot, thereafter, showed marked improvement, and she left the hospital without amputation on March 16, 1955 about four months after admission. The foot has continued to heal, and she has had no recurrence of her infection.

DISCUSSION

The foregoing cases illustrate what can be accomplished by the application of sound principles of management of diabetes and of surgical management of infections. It should be emphasized that in most instances, unless there is good local drainage with subsequent healing of the feet, the patient will have to undergo high amputation. Time is of the essence and early, adequate drainage must be achieved. If there is a delay of even a week, infection under pressure may destroy the foot, and one is left with no alternative except a mid-thigh amputation with its usual crippling result. There is no need for early high amputation as a life-saving measure, since antibiotics have obviated the likelihood of ascending infection. This does not mean that we can afford to be leisurely in dealing with the local lesion.

In the case of elderly diabetics in whom high amputation is necessary but who appear to have the mental and physical equipment for adjusting to a prosthetic life, it is well to start immediately after the operation with proper bandaging of the stump, in order to achieve a conical shape which will fit a prosthesis. The stump should be exercised, and the patient should be instructed to lie prone in order to prevent any flexion deformity of the stump. In recent years we have recommended below-the-knee amputations in patients who are candidates for a prosthesis and who have a good popliteal pulse. We believe that these patients attain better ambulation if they retain their knee joint.

SUMMARY AND CONCLUSIONS

1. Peripheral vascular disease is a common complication in elderly diabetics, since diabetes accelerates the aging process.

2. Treatment of foot infections should consist of good diabetic and nutritional management, wide local drainage of infections, and administration of antibiotics. High amputations for infections should be performed only if there is failure of conservative treatment after two weeks' trial.

3. Gangrene carries a poorer prognosis for preservation of limbs. Even in the case of gangrene, however, limited amputation (digital or transmetatarsal) may give the patient a serviceable foot for a time.

4. Sympathectomy has little to offer the elderly diabetic with peripheral vascular disease.

REFERENCES

1. Hurwitz, D.: Management of lesions of the feet in diabetes, *Diabetes* **4:** 107–109 (Mar.–Apr.) 1955.
2. Pratt, G. H.: Amputation after surgical sympathectomy for obliterative vascular disease; incidence after 309 sympathectomies, *Surg., Gynec. & Obst.* **100:** 43–50 (Jan.) 1955.
3. Berry, R. E.; Flotte,C. T., and Coller, F. A.: A critical evaluation of lumbar sympathectomy for peripheral arteriosclerotic vascular disease, *Surgery* **37:** 115–129 (Jan.) 1955.

MORTALITY AMONG THE MARRIED

DEWEY SHURTLEFF, M.P.H.

Arlington, Virginia*

Married persons, on the average, live longer than the single, widowed or divorced. This interesting aspect of the marital state has been verified again by the U. S. mortality experience for the three-year period 1949 through 1951 (1).

POPULATION BASE

The census of 1950 (2) provided the necessary population bases for the detailed classification of mortality by marital status. At the time of enumeration, the question was asked, "Is he (she) now married, widowed, divorced, separated, or has he never been married?" Persons classified as married were those married only once or remarried after having been widowed or divorced. Also included among the married were those reported as separated—persons with legal separations, persons living apart with intentions of obtaining a divorce, and other persons permanently or temporarily estranged from their spouses because of marital discord. Those reported as never married or with annulled marriages were classified as single.

Table 1 shows the distribution of the population by marital status for each age-sex group. Most men 20 to 24 years old were single; but by the time they were 25 to 29 years old, 3 out of 4 were married. Women married younger; 2 out of 3 were married at ages 20–24, and 4 out of 5 at ages 25–29. The peak percentage married was 87.1 for men at 40–44 years and 86.2 for women at 30–34. From 35 years on for men and from 30 years on for women the proportion single in the population remained nearly constant, close to 10 per cent. The proportion widowed increased with advancing age, much more so for women than for men. The peak percentage divorced was 3.0 for men at ages 50–54 and 3.7 for women 40–44.

MORTALITY DATA

Marital status at time of death is regularly reported on the death certificate, along with age, race and sex. Deaths classified in the same categories as the enumerated population are now available for 1949, 1950 and 1951 (3). Rates shown in this paper are based on the average annual number of deaths (numerator) occurring in this three-year period and on the population (denominator) enumerated in the 1950 census.

Misreporting of marital status likely happens both in the census and on the death certificate, and this will affect the death rate. Since it is probable that some divorced persons are enumerated as single, married, or widowed, the census returns doubtless understate somewhat the actual number of divorced persons who have not remarried. On the other hand, the considerations leading an individual to misrepresent his marital status to the enumerator may not

* Address: 4108 North 25th St., Arlington 7, Va.

TABLE 1

Percentage Distribution of the Population by Marital Status, According to Age and Sex: United States, 1950

Sex and Age (yrs.)	Single	Married	Widowed	Divorced
Men				
20 and over	17.0	76.1	4.7	2.2
20–24	59.1	39.9	0.2	0.9
25–29	23.8	74.2	0.3	1.7
30–34	13.2	84.3	0.4	2.1
35–39	10.1	86.8	0.7	2.4
40–44	9.0	87.1	1.2	2.7
45–49	8.7	86.2	2.1	2.9
50–54	8.3	85.0	3.7	3.0
55–59	8.3	83.1	5.9	2.7
60–64	8.6	79.3	9.6	2.5
65–69	8.7	74.0	15.0	2.3
70–74	8.3	67.5	22.2	1.9
75–79	8.1	59.0	31.4	1.5
80–84	7.4	48.2	43.3	1.1
85 and over	7.7	33.6	57.9	0.8
Women				
20 and over	11.8	72.3	13.3	2.7
20–24	32.3	65.6	0.4	1.7
25–29	13.3	83.3	0.9	2.5
30–34	9.3	86.2	1.6	3.0
35–39	8.4	85.5	2.7	3.5
40–44	8.3	83.1	5.0	3.7
45–49	7.9	79.8	8.6	3.6
50–54	7.7	75.0	13.9	3.3
55–59	7.7	69.1	20.5	2.7
60–64	8.2	60.1	29.7	2.1
65–59	8.4	48.9	41.1	1.5
70–74	9.0	36.6	53.3	1.1
75–79	9.4	24.7	65.1	0.7
80–84	9.4	14.2	75.9	0.5
85 and over	9.7	7.0	82.9	0.4

Source: Table 102 of reference 2.

apply after his death. Furthermore, the personal information on the death certificate may be supplied by the decedent's relative, who presumably has accurate information. If the number of decedents reported as divorced is too small, probably it is not as deficient as the number of divorced persons returned in the census. The effect on the death rates is to make them too high for the divorced.

Misstatements about marital status, it can reasonably be assumed, occur mostly among individuals living alone. For example, the married man living apart from his wife may report himself as single. Errors of this kind would tend to swell the true number of single men and thus to lower their death rate. On the other hand, although such errors would reduce the true number of married men, the number of wandering husbands would have to be large to affect appreciably the death rate for married men, since the bulk of the adult population is married.

Besides, of those reported in 1950 as married, 95 per cent were living with their spouse (4).

MORTALITY BY MARITAL STATUS, AGE AND SEX

All through the age span shown in Table 2, for men and for women, the death rates are lower for the married than for the single, widowed, or divorced. For both men and women in every age group 20 years and over, the mortality rank-order of three of the marital classes remains the same—the lowest for the married and the highest for the divorced, with the single in between. The rank-order of the widowed class shifts with advancing age. At the early ages, the death rate for widowers is the highest of the four marital classes, but beyond 45 years is below that for divorced men, and beyond 60 is below that for single men. A similar pattern is seen for women, with the shift occurring fifteen years later in life.

For each of the four marital classes, the death rates for men are higher than those for women in every age group between 20 and 84. This is shown in Figure 1, in which the age-specific death rates for males of each marital class are expressed as percentages of the death rates for females of corresponding marital class and age. The largest percentage difference in rate between the sexes appears for the divorced in the age groups under 60, and then for the single in the age groups 60 and over. The smallest difference appears in each age group for the married. From 25 to 64 years, in each age group, the rate for widowers is close to double that for widows. The ratios for the other marital classes, beginning at 25–34 years, rise to peaks in middle age—2.9 for the divorced at ages 45–54, 2.6 for the single, and 1.7 for the married at ages 55–59. Then, with advancing age, all four ratios decline and converge, until at age 80–84 the death rates for men are 1.2 times those for women among the married and divorced, 1.3 among the widowed, and 1.4 among the single.

An index of mortality for males and females of each marital class is convenient for summarizing the series of age-specific death rates for a marital class and for comparing the mortality of one marital class with another. When the age structures of the four populations differ widely, as seen in Table 1, direct comparisons of crude death rates are practically useless. The differences in the distribution by age of the marital groups can readily be taken into account by some method of age-standardization. The method used here is to calculate the number of deaths expected in a standard population experiencing the age-specific death rates for the marital class.

If the 1949–51 death rates for age 20 and over by marital status, age and sex had occurred in a standard population distributed by age like the population for each sex enumerated in 1940, taking the expected number of deaths for the married as 100, the index numbers would be:

	Single	Married	Widowed	Divorced
Men	163	100	185	207
Women	124	100	155	155

TABLE 2

Average Annual Death Rates by Marital Status, Age, and Sex: United States, 1949–51

(Exclusive of deaths among armed forces overseas. Rates per 1,000 population in each specified group enumerated as of April 1, 1950.)

Age (yrs.)	Men					Women				
	Total*	Single	Married	Widowed	Divorced	Total*	Single	Married	Widowed	Divorced
20–24	1.9	2.2	1.5	5.7	3.4	1.0	1.2	0.9	3.4	1.7
25–34	2.2	3.6	1.7	8.6	5.8	1.4	2.2	1.2	4.1	2.6
35–44	4.3	8.5	3.6	12.1	11.8	2.9	3.9	2.6	6.2	4.5
45–54	10.7	17.8	9.3	21.6	23.2	6.5	7.0	5.7	10.3	8.1
55–59	20.0	30.0	17.8	30.4	36.5	11.4	11.5	10.2	14.8	13.8
60–64	29.0	41.0	25.8	39.5	48.6	17.5	16.6	15.7	20.7	21.1
65–69	41.1	55.0	36.5	50.0	66.1	26.0	24.8	23.5	28.1	33.1
70–74	60.4	78.8	54.3	69.1	91.9	43.2	42.3	39.0	44.8	58.2
75–79	90.1	111.7	80.8	98.5	142.3	69.8	71.0	63.1	70.7	99.5
80–84	132.3	159.6	118.9	139.6	208.0	110.6	117.2	98.9	110.0	170.1
85 and over	215.8	204.8	188.9	231.0	310.4	192.6	186.8	144.8	194.1	211.5

* Includes deaths for which marital status was not stated.

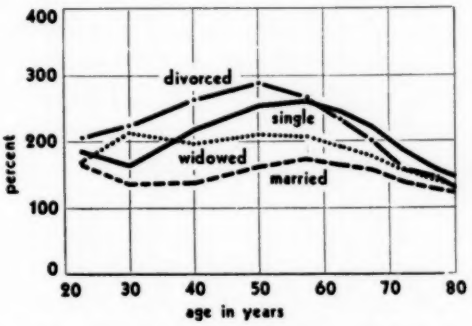

FIG. 1. Age-specific death rates for men of each marital class as percentages of corresponding rates for women: United States, 3-year average, 1949–51.

Plotting points:

Age	Single	Married	Widowed	Divorced
22.5	187	165	169	203
30	164	137	211	223
40	217	139	196	262
50	254	161	209	287
57.5	260	174	206	265
62.5	246	165	191	231
67.5	222	156	178	200
72.5	186	139	154	158
77.5	157	128	139	143
82.5*	136	120	127	122

* These values are not shown on the graph. They are used to fix the curves up to age 80.

These figures summarize the mortality differences among the marital classes. The married have the most favorable mortality, and the single have a lower mortality than either the widowed or divorced. Differences in mortality between married and unmarried are greater for men than for women.

SPECULATION

Up to this point facts have been presented to show the marked differences in death rates for the single, widowed and divorced compared with rates for the married. Authorities interested in this subject have suggested a number of factors to explain why married people live longer, and some small-scale studies have been carried out to obtain measures of a few of these. In what follows, an attempt will be made to show how the mortality data support the suggestions. The factors to be mentioned are not intended to be exhaustive, but rather to be provocative. They represent the author's own selection; many others will occur to the thoughtful reader. More extensive data representing much more research will be needed in order to test the importance or validity of the various opinions offered.

SELECTION

Speculation about why married people live longer than unmarried people involves a consideration of the effect of various factors. For example, selection is one of the well-known conditions influencing the mortality experience of a group of people. What kind of people get married, and in what ways are they different from people who avoid marriage? Although the favorable mortality experience of married persons follows, at least in part, from the marriage environment, it may result from the standards of personal and medical examination preceding selection of a spouse. Self-selection may occur; for instance, a man who considers himself to be in poor health may be less likely to contract for the responsibilities of married life. Since selection plays a part again in remarriage, healthy persons are more likely to be chosen as partners than the ailing, leaving those who remain widowed and divorced the poorer mortality risks. The difference in death rates between married people and unmarried people may thus arise, not from any particular hazard of the unmarried state, but rather from this element of selection whereby the frailer men and women tend to avoid marriage. That such a process is happening may be deduced from the age-specific rates. If the unmarried state tends to attract the less hardy, this fact should be reflected in relatively high death rates early in their adult life.

The evidence for selection as a factor in the lower mortality of the married may be seen more clearly by examining the relative differences in rates between the unmarried and the married at each age. Taking the mortality of the married as 100 in each age group, Figure 2 shows the age-specific death rates for the single, widowed and divorced, expressed as percentages of the corresponding rate for the married. The percentile differences are greatest between married and unmarried men between the ages of 25 and 44, presumably when family responsibilities are greatest. Similarly, the percentile differences between married and unmarried women are greatest between the ages of 25 and 34. Evident in the

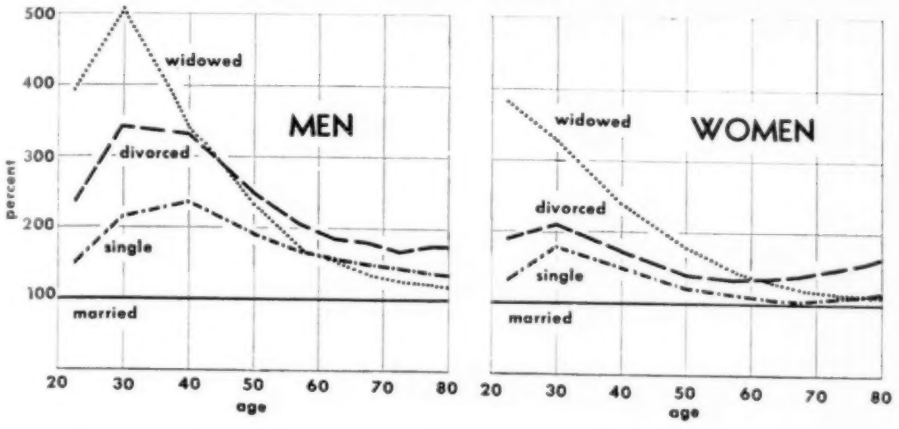

FIG. 2. Comparative mortality by marital status. Age-specific death rates for each marital-sex class as percentages of corresponding rates for married persons: United States, 3-year average, 1949–51.

Plotting points:

Age	Men				Women			
	Sing.	Marr.	Wido.	Divo.	Sing.	Marr.	Wido.	Divo.
22.5	149	100	392	233	132	100	384	190
30	215	100	507	343	180	100	329	211
40	237	100	339	332	151	100	239	175
50	192	100	233	250	122	100	179	141
57.5	168	100	170	205	113	100	144	135
62.5	159	100	153	188	106	100	132	135
67.5	151	100	137	181	105	100	120	141
72.5	145	100	127	169	108	100	115	149
77.5	138	100	122	176	112	100	112	158
82.5*	134	100	117	175	118	100	111	172

* These values are not shown on the graph. They are used to fix the curves up to age 80.

low mortality rates of the married early in married life is the robustness of husbands and wives.

ENVIRONMENT

Persistent differences in rates between married and unmarried, seen in Figure 2 throughout the age span, suggest that the married state itself may directly affect mortality. Family routine may be conducive to regularity in the pattern of eating, sleeping, working and playing. Family responsibilities may call for moderation. The single person may work in relatively more hazardous jobs and indulge more freely in extremes in his living habits. The stabilizing influences of family living may be greater for the adventuresome male (Fig. 1), because society and perhaps temperament limit the behavior pattern of the unmarried man less than the unmarried woman. Also, married people may have stronger motivation to guard their health for the sake of their partners and dependents.

Mutual concern of partners may lead them to seek medical services earlier when symptoms appear.

As divorce in the United States has become more acceptable in the social pattern, indications are stronger that married people are able to adjust to and/or find satisfaction in the married state. Both widowed and divorced have suffered disruptions of family life with the accompaniment of deep emotional and mental strain. Those who fail to remarry may lose the stabilizing influences of family life, and perhaps are reduced in social and economic status.

MORTALITY BY CAUSE

Further speculation about why married people live longer than unmarried people is afforded by examining how mortality among the marital classes varies by cause of death (5). To facilitate comparison, index numbers have been computed in the same manner as previously described on page 656, except that the age adjustment is made for the population age 20 to 74 years. Summarized in Table 3 are the mortality differences among the marital classes for selected causes. The index numbers shown in the table for "all causes" are not identical with the index numbers listed in the tabulation on page 656, because the death rates for the age group 75 years and over were not used in computing the standardized numbers of deaths in Table 3.

Perhaps the most striking feature of Table 3 is that for every cause shown, mortality varies by marital status, *i.e.*, there is no disease that kills impartially, that kills the married and the unmarried alike. What would be the characteristics of such a disease if it exists? Surely one important feature would be high fatality—once it struck there could be no escape just because the victim immediately sought medical attention. Risk of death from the disease must be everywhere the same, regardless of the status of nutrition, work, recreation, housing, income, medical care and location. Such a disease could be acute or chronic, but it must strike without warning. Symptoms of the disease, if chronic, should not be evident to mark the victim as a poor marital risk. In short, the factors of selection and of socio-economic environment would have to be inoperative if mortality from this cause were to be the same among the marital classes.

Leukemia exhibits less variation in mortality by marital status than any of the other causes in Table 3. A tempting suggestion is that socio-economic factors are not associated with the incidence of this fatal disease of the blood-forming organs. Whether discovery of leukemia in a person has any effect on his subsequent marital status is problematical. The effect, if it exists, is certainly small. If deaths from leukemia are truly independent of marital status, then the small variation noted in Table 3 for this disease might well reflect errors of reporting for the widowed and divorced in the census and on the death certificate, such as previously discussed.

For some of the causes listed in Table 3—tuberculosis, syphilis, influenza and pneumonia, cirrhosis of liver, accidents, suicide and homicide—mortality among the unmarried is much higher than among the married. Deaths from these

TABLE 3

Standardized Number of Deaths from Selected Causes for Single, Widowed, and Divorced Persons as Percentage of Corresponding Number for Married Persons: United States, 1949–51

(Numbers after causes of death are category numbers of the Sixth Revision of the International Lists, 1948)

Cause of Death	Men				Women			
	Single	Married	Widowed	Divorced	Single	Married	Widowed	Divorced
All causes	172	100	200	218	119	100	162	149
Tuberculosis, all forms 001–019	410	100	537	498	225	100	345	242
Syphilis and its sequelae 020–029	229	100	288	375	124	100	249	270
Malignant neoplasms 140–205	136	100	144	156	121	100	135	139
Of buccal cavity and pharynx 140–148	217	100	183	257	93	100	152	150
Of digestive organs and peritoneum 150–156A, 157–159	143	100	150	147	114	100	129	126
Of respiratory system 160–164	140	100	153	193	112	100	124	166
Of breast 170	175	100	290	114	159	100	119	125
Of genital organs 171–179	109	100	138	130	106	100	165	172
Of urinary organs 180, 181	127	100	127	150	106	100	126	129
Of other, and unspecified sites 156B, 165, 190–199	138	100	137	150	119	100	124	129
Leukemia and aleukemia 204	98	100	113	115	100	100	111	122
Lymphosarcoma and other neoplasms of lymphatic and hematopoietic tissues 200–203, 205	102	100	112	125	122	100	126	107
Benign neoplasms and neoplasms of unspecified nature 210–239	146	100	167	157	124	100	140	134
Diabetes mellitus 260	144	100	157	169	60	100	126	96
Anemias 290–293	217	100	194	190	161	100	142	153
Vascular lesions affecting central nervous system 330–334	144	100	185	175	100	100	152	131
Diseases of the heart 410–443	147	100	157	176	111	100	155	144
Chronic rheumatic heart disease 410–416	164	100	162	175	140	100	131	138
Arteriosclerotic heart disease, including coronary disease 420	131	100	134	165	105	100	142	146
Non-rheumatic chronic endocarditis and other myocardial degeneration 421, 422	235	100	225	236	151	100	179	155
Other diseases of heart 430–434	209	100	258	284	127	100	189	159
Hypertension with heart disease 440–443	148	100	210	164	91	100	175	132
Hypertension without mention of heart 444–447	130	100	209	152	95	100	181	130
General arteriosclerosis 450	240	100	217	253	161	100	188	192
Chronic and unspecified nephritis and other renal sclerosis 592–594	158	100	203	160	108	100	173	119
Influenza and pneumonia 480–493	331	100	327	362	205	100	227	174
Bronchitis 500–502	195	100	226	228	154	100	140	134
Ulcer of stomach and duodenum 540, 541	193	100	182	241	166	100	154	175
Appendicitis 550–553	136	100	133	137	125	100	130	124

TABLE 3—(*Continued*)

Cause of Death	Men				Women			
	Single	Married	Widowed	Divorced	Single	Married	Widowed	Divorced
Hernia and intestinal obstruction 560, 561, 570	228	100	200	196	123	100	142	132
Cirrhosis of liver 581	268	100	282	477	90	100	208	230
Acute nephritis and nephritis with edema, including nephrosis 590, 591	164	100	197	197	122	100	231	147
Hyperplasia of prostate 610	151	100	170	167	—	—	—	—
Deliveries and complications of pregnancy, childbirth, and the puerperium 640–689	—	—	—	—	29	100	111	65
Abortion 650–652	—	—	—	—	55	100	312	206
All other complications 640–649, 660–689	—	—	—	—	26	100	88	49
Motor-vehicle accidents E810–E835	181	100	308	346	105	100	252	251
All other accidents E800–E802, E840–E962	215	100	256	318	158	100	220	223
Suicide E963, E970–E979	211	100	334	382	123	100	190	286
Homicide E964, E980–E985	181	100	554	369	93	100	431	297
All other causes Residual	228	100	241	278	153	100	171	153

causes are regarded by sociologists as correlated with socio-economic factors. The real problem here is to distinguish cause and effect. Does the existence of the disease lead to the particular marital status? Or is it the other way round? Does the marital status lead to the occurrence of violence, or vice versa?

Tuberculosis. Deaths from tuberculosis have long been associated with sub-standard socio-economic factors, such as improper diet, lack of rest, and poor sanitation. Differences between the married and the unmarried in mortality from tuberculosis are especially large in early adult life, as shown in the following tabulation. The death rates for tuberculosis for the single, widowed, and divorced in each age group have been expressed in the form of ratios to the corresponding rate for the married.

Age	Men			Women		
	Single	Widowed	Divorced	Single	Widowed	Divorced
20–24	2.2	8.1	2.6	1.9	5.7	2.2
25–34	4.3	12.7	5.2	2.9	4.9	3.0
35–44	5.1	7.7	6.5	2.5	3.4	2.6
45–54	4.6	5.0	5.8	2.0	2.5	2.0
55–59	3.8	3.2	5.0	1.8	1.8	2.0
60–64	3.7	2.8	4.2	1.7	1.5	1.9
65–69	3.1	2.1	3.3	1.6	1.3	1.8
70–74	3.1	1.8	3.1	1.4	1.1	2.3

Especially high are the death rates among young widowed persons; rates for widows are five to six times the rate for wives, and rates for widowers are eight to thirteen times those for husbands. Marital infection can reasonably be expected to affect the mortality of the widowed from communicable diseases. Once tuber-

culosis has attacked, the widowed person may lack the necessary encouragement to undergo the lengthy treatment and restricted behavior necessary to effect a cure. For the widowed tuberculous patient who is left with the entire responsibility of dependent children, accepting isolation for sanatorium treatment often involves severe economic and emotional strain.

The chances of the bachelor dying from tuberculosis are two to five times those of a husband. The question is, Does he remain a bachelor because he has tuberculosis, or did he contract tuberculosis because he never married? Is not the tuberculous man who marries likely to live longer than if he had remained single, because he usually leads a more regular life? Similar considerations apply to the divorced man, whose chances of dying from tuberculosis are three to six times those of a husband.

Syphilis and its sequelae. Social controls and conventions restrict the sex relations of the unmarried, especially the unmarried man, less than the married. Mortality from a disease associated with promiscuous behavior would be expected to be higher among the unmarried than among the married, whose extramarital relations are censured by society and are sufficient grounds for divorce. As seen in the mortality record, the widowed and the divorced are special targets for syphilis. The death rates for divorced men are five times those for husbands at ages 25 to 44, four times at ages 45 to 69, and three times at ages 70–74. The death rates for widowers are nine times those for husbands at ages 25–34, six times at 35–44, three times at 45–59, two times at 60–69, and nearly one and a half times at 70–74. The ratios of rates for widows and divorcees to rates for wives follow similar patterns seen for the men, but the differences are not as pronounced. Whereas the death rates for bachelors remain twice those for husbands at ages 25 to 74, after 55 the rates for spinsters drop below those for wives.

Influenza and pneumonia. The death rates for this cause, as in the case of tuberculosis and of syphilis, are much higher for single, widowed, and divorced men in each age group than the rates for husbands. Apparently, the man who is under the firm control of his wife exposes himself much less to the danger of respiratory disease, or he has much better care after he contracts a respiratory ailment.

Cirrhosis of the liver. Alcohol can be an important factor in deaths from cirrhosis of liver. Between the ages 35 and 74, death rates for men are double those for women. During these ages, death rates for single and widowed men are two to four times those for husbands, whereas the rates for divorced men are two to eight times those for husbands.

Excessive drinking can be an important cause of divorce. This connection may offer a partial explanation of the high death rates from cirrhosis of the liver among the divorced. At 25–34 years, the rates for divorcees are more than five times those for wives, and the rates for divorced men are more than ten times those for husbands.

Accidents. The daring male lives more dangerously than does the female, as shown by accident fatalities. At ages 20 to 34 the rates for men are five times

those for women. With advancing age this difference lessens, until at 75–84 years the rates are practically the same for the two sexes. Apparently married life tames the bold male, reducing his chance of dying from accident to less than half that of the unmarried man throughout most of his span of life.

Suicide rates are three times higher for men than for women in early adult years and rise with advancing age until they are seven times higher for men than for women at ages 75 and over. Stability of the married state plays a major part in the much lower suicide rates for husbands—half or less throughout the age span than the rates for single, widowed, or divorced men. The divorced group suffers the highest suicide rates, the rates for divorcees being two to four times those for wives and the rates for divorced men being three to five times those for husbands. To some extent suicide among the divorced may stem from frustrations in life after broken marriage ties and to some extent from the existence of a high proportion of unstable personalities among the divorced.

Homicide rates are highest at ages 25 to 34, with rates for men three times those for women. In this age group the rates for single, divorced, and widowed men are two, four, and seven times the rate for husbands. The rate at 25 to 34 years for spinsters is only slightly higher than that for wives, whereas the rates for divorcees and widows are 3.5 and 5.5 times that for wives. On the average, single women are safest from homicidal attack.

Of the causes discussed so far, four appear in the list of the ten leading causes of death for 1950 in the United States at ages 20 and over—accidents, influenza and pneumonia, tuberculosis, and suicide (6). Unlike the figures for these causes, the mortality differences among the marital classes seen in Table 3 are not so pronounced for the three leading causes of death—diseases of the heart, malignant neoplasms, and vascular lesions affecting central nervous system. For these three, the differences in mortality for the single, widowed, and divorced compared with the married fall below the average differences for all causes.

Diseases of the heart claim more lives in the United States than any other cause of death. Among men the leading cause of death is accidents, under the age of 35; thereafter diseases of the heart rank first. Among women the leading cause of death is accidents under the age of 25; from 25 to 54 years the first rank is held by malignant neoplasms, and after 54 by diseases of the heart. At every age, the death rates for diseases of the heart are higher for men than for women; the rates at ages 35 to 64 are especially high for men—more than double those for women.

Throughout the age span of 20 to 84 years, for both men and women, death rates for diseases of heart are lower for the married than for the single, the widowed, or the divorced. For young adults, the death rate for the married is half that for the single or divorced. Death rates for the widowed are five times those for the married during the younger years. In middle and old age the mortality of spinsters is only slightly higher than that of wives, whereas the death rates for bachelors remain 1.4 times as high as for husbands. This hints that the tranquilizing influences of married life have a profound effect on the adventuresome male.

For nearly all the causes listed in Table 3, the married have the more favorable

mortality. An obvious exception involves deliveries and the complications of pregnancy, childbirth and the puerperium. Aside from these maternal causes of death among the married, mortality among spinsters is lower than among wives for a few causes: malignant neoplasm of the buccal cavity and pharynx, diabetes, hypertension, cirrhosis of the liver, and homicide.

Diabetes mellitus is one of the few diseases for which mortality among women is greater than among men. The sharp difference between the sexes arises only among the married and widowed. The spinster seems to be less susceptible than the bachelor, and the divorcee about as susceptible as the divorced man. Beginning in the age group 45–54, death rates for spinsters are eight-tenths to one-half the rates for wives. This suggests that wives are economically in better circumstances than spinsters and are more likely to be overnourished. Perhaps a better suggestion is that wives are much more involved in the handling of food for meal preparation and as a consequence are exposed to much greater risk of becoming overweight.

Several diseases are associated with obesity. Diabetes, cirrhosis of the liver, and some diseases of the cardiovascular-renal complex—hypertension, arteriosclerosis, vascular lesions affecting the central nervous system, and chronic nephritis—are in some way or other enhanced by obesity. Whether wives tend to be more obese than spinsters is unknown, but the age-specific death rates from these causes follow a common pattern: Beginning in the age group 45–54, death rates for spinsters are the same as, or lower than those for wives. The ratios of death rates from these causes for spinsters in each age group to the corresponding rate for wives are:

Cause of Death

Age	Diabetes Mellitus	Vascular Lesions Affecting CNS	Arteriosclerotic Heart Disease, etc.	Hypertension with Heart Disease	Hypertension; No Mention of Heart	Chronic Nephritis, etc.	Cirrhosis of the Liver
20–24	1.5	1.3	1.1	1.2	1.3	1.4	4.0
25–34	2.5	1.4	1.7	1.4	1.4	1.8	1.6
35–44	1.7	1.2	1.4	1.3	1.1	1.3	1.1
45–54	.8	1.0	1.1	.9	.9	1.0	.9
55–59	.6	1.0	.9	.8	.8	.9	.8
60–64	.4	1.0	1.0	.9	.8	1.0	.7
65–69	.4	.9	1.0	.9	.9	.9	.7
70–74	.5	1.0	1.1	.9	1.0	1.0	.8

For only four other causes listed in Table 3 is the foregoing pattern seen among women—syphilis, leukemia, motor-vehicle accidents, and homicide. Also, beginning in the age group 45–54, the death rates for diabetes are lower for divorcees than for wives.

SUMMARY

Married persons, on the average, live much longer than the unmarried. Among both men and women at every age, the married have lower death rates than the

single, widowed, or divorced. When allowance is made for differences in age distribution of the marital classes, the mortality of bachelors is two-thirds greater than that of husbands, and the mortality of widowed and divorced men is double that of husbands. The advantage of the married state is not as marked among women. The mortality of spinsters is a fourth again as high as that of wives, and the mortality of widows and divorcees is half again as high. Examination of how mortality among the marital classes varies by age, sex, and cause of death provides a basis for some speculation upon the nature of selection of persons into the marital groups and the effect of marriage itself on mortality rates.

REFERENCES

1. SHURTLEFF, D.: Mortality and marital status, *Public Health Reports* **70:** 248–252 (March) 1955.
2. U. S. Bureau of the Census: U. S. Census of Population, 1950. Vol. II. Characteristics of the Population, Part 1, United States Summary. Washington, D. C., U. S. Government Printing Office, 1953.
3. National Office of Vital Statistics: Vital Statistics of the United States, 1949, Part I; 1950, Vol. III; 1951, Vol. II. Washington, D. C., U. S. Government Printing Office, 1951, 1953, 1954.
4. Table 104, reference 2.
5. National Office of Vital Statistics: Mortality from Selected Causes, by Marital Status, Age, Race, and Sex: United States, 1949–51. Vital Statistics—Special Reports, vol. 39, No. 7. Washington, D. C., 1956.
6. National Office of Vital Statistics: Leading Causes of Death: United States and Each State, 1950. Vital Statistics—Special Reports, vol. 37, No. 15. Washington, D. C., 1953.

ELECTROPHORETIC SERUM PROTEIN PATTERNS IN THE AGED*

J. L. KAREL, B.Sc., V. M. WILDER, Ph.D. and M. BEBER, M.D., Ph.D.

The Department of Biochemistry, University of Nebraska College of Medicine, Omaha, Nebraska

Experience in the investigation of blood proteins has shown that electrophoretic methods possess great advantages in the evaluation of the status of plasma or serum proteins under normal conditions or in various diseases. Since there is a definite need for information of this type in the field of geriatrics, it was the purpose of this investigation to study the possible changes in the electrophoretic pattern of the serum proteins in a group of normal aged people. This approach permits the evaluation of blood protein fractions in terms of relative and absolute concentration and electrophoretic mobility. Certain limitations of the method and qualifications in the evaluation of results will be explained throughout the following discussion.

MATERIAL AND METHODS

The 21 subjects studied in this series were free from known pathologic processes which might affect the serum protein patterns. All were considered to be receiving an adequate diet. There were 19 males and 2 females, with ages ranging from 66 to 88; the mean age for the group was 74.

All blood samples were collected in the fasting state before breakfast. After the blood had clotted at room temperature, the serum was decanted, centrifuged to remove the remaining erythrocytes, and stored at 4°C. until used. Most sera were analyzed within twenty-four hours after obtaining the blood samples.

The buffer employed in this study was composed of sodium diethyl-barbiturate-diethyl-barbituric acid (NaV-HV or Veronal buffer) with a pH of 8.55 at 25°C. and an ionic strength of 0.1. Attempts were made to maintain a uniform concentration of protein in the solution being analyzed, since it has been shown that protein concentration has important effects upon the percentage distribution and the mobility of the components observed in the electrophoretic pattern (1, 2). In about half the experiments the serum was diluted with buffer to a protein concentration of 2.8 per cent; in the remainder the serum was diluted 1:3 with buffer, resulting in a protein concentration in the range of 2.0 to 2.3 per cent. The Aminco portable electrophoresis apparatus, which employs a cylindrical-lens system, was used in this investigation. All runs were made at 12.5 mA, which yielded a potential gradient of 5.39 volts $cm.^{-1}$ (with slight variations between batches of buffer). The time of the average run was three hours, which permitted a maximum resolution of the components.

The initial boundaries in each experiment were photographed on the same plate used to record the final pattern. The electrophoretic patterns were enlarged three times and traced onto smooth white paper for measurement of the curves according to the method of Tiselius and Kabat (3). For practical purposes, the relative concentration of the components and the electrophoretic mobilities were determined from the ascending boundary patterns (4). The calculations of mobility were made using factors derived from

* Taken in part from a thesis by J. L. Karel presented in partial fulfillment of the requirements for the degree of Master of Science.

the standardization of the ascending limb of the cell with purified bovine serum albumin of known mobility (courtesy of Armour and Company).

Total serum protein concentration was determined by a modification of the biuret method of Levin and Brauer (5).

In order to compare our findings in these 21 normal aged people with those in a lower-age group, serum from 9 normal, younger individuals (22 to 50 years) was studied under identical conditions.

RESULTS AND DISCUSSION

A. The appearance of the patterns in the aged normal group

All of the patterns showed excellent resolution into five components: albumin, alpha-1 globulin, alpha-2 globulin, beta globulin, and gamma globulin. Under the conditions of the experiment, about half of the patterns showed the separation of a distinct, gamma-1 globulin component which migrated between the beta globulin and gamma globulin fractions and appeared only on the descending boundary patterns. The concentration of this component was measured in only

TABLE 1

Serum Protein Patterns of the Aged Normal Group

Subjects	Tot. Serum Protein (Gm./100 ml.)	A/G	Per Cent of Total Protein						Grams per 100 ml. Serum					
			Albumin	Alpha 1	Alpha 2	Beta	Gamma 1*	Tot. gamma	Albumin	Alpha 1	Alpha 2	Beta	Gamma 1*	Tot. gamma
J. A.	4.80	0.90	47.52	5.96	11.06	19.15	3.10	16.31	2.28	0.29	0.53	0.92	0.15	0.78
J. G.	5.47	1.07	51.51	3.60	14.82	17.41	3.67	12.66	2.82	0.20	0.81	0.95	0.20	0.69
C. G.	7.43	0.97	49.08	5.96	13.76	13.76		17.43	3.65	0.44	1.02	1.02		1.30
R. H.	6.52	1.33	57.04	4.06	10.60	15.53	2.87	12.77	3.72	0.27	0.69	1.10	0.19	0.83
B. H.	6.35	0.56	35.91	6.78	12.47	22.22		22.63	2.28	0.43	0.79	1.41		1.44
O. H.	6.74	0.74	42.73	7.36	12.21	18.62		19.09	2.88	0.50	0.83	1.25		1.29
Ed. J.	5.28	0.65	39.30	11.49	12.92	20.89		15.40	2.08	0.61	0.68	1.10		0.81
E. J.	5.50	1.22	54.92	5.24	12.64	19.80	1.60	7.40	3.02	0.29	0.70	1.09	0.09	0.41
J. K.	6.45	0.80	44.36	4.91	12.73	19.27		18.73	2.86	0.32	0.82	1.24		1.21
J. L.	6.91	0.74	42.57	5.63	15.15	18.61		18.04	2.94	0.39	1.05	1.29		1.25
O. L.	5.96	1.10	52.51	5.18	14.94	15.53	2.32	11.83	3.13	0.31	0.89	0.93	0.14	0.71
A. L.	5.24	0.60	37.84	10.50	15.54	15.54	3.43	20.58	1.98	0.55	0.81	0.81	0.18	1.08
C. L.	4.80	0.96	48.91	5.35	8.39	14.96	3.58	22.38	2.35	0.26	0.40	0.72	0.17	1.08
H. M.	6.78	1.18	54.11	5.38	11.76	13.17		15.58	3.67	0.36	0.80	0.89		1.06
G. P.	6.39	0.93	48.21	6.46	12.05	17.07		16.21	3.08	0.41	0.77	1.09		1.04
F. S.	5.65	0.68	40.27	6.76	16.22	21.08	3.97	15.68	2.28	0.38	0.90	1.19	0.22	0.89
S. S.	6.71	0.76	43.15	7.32	12.77	17.60	2.76	19.16	2.90	0.49	0.86	1.18	0.19	1.29
H. T.	6.74	0.72	41.82	4.94	8.67	9.55	4.83	30.19	2.82	0.33	0.58	0.64	0.33	2.03
D. U.	6.19	0.73	42.34	6.16	9.95	17.69	5.12	23.85	2.62	0.38	0.62	1.08	0.32	1.48
F. V.	5.80	0.93	48.19	5.56	13.61	18.89	3.60	13.75	2.80	0.32	0.79	1.10	0.21	0.80
E. Y.	6.03	0.83	45.25	7.67	14.26	17.48		15.34	2.73	0.46	0.86	1.05		0.93
Mean	6.08	0.88	46.07	6.30	12.69	17.33	3.55	16.17	2.80	0.38	0.77	1.05	0.20	1.07

* Measured only in descending column.

12 patterns. The other patterns showed it, but the amount was not definite enough for measurement, and in a few cases it was not resolved.

The relative and absolute concentrations of the serum protein fractions are recorded in Table 1 and the electrophoretic mobilities are shown in Table 3.

TABLE 2

Serum Protein Patterns of the Younger Normal Group

Subjects	Tot. Serum Protein (Gm./100 ml.)	A/G	Per Cent of Total Protein						Grams per 100 ml. Serum					
			Albumin	Alpha 1	Alpha 2	Beta	Gamma 1*	Tot. gamma	Albumin	Alpha 1	Alpha 2	Beta	Gamma 1*	Tot. gamma
S. F.	6.32	1.40	57.87	4.06	9.01	16.62	2.28	12.44	3.66	0.26	0.57	1.05	0.14	0.79
J. K.	6.61	1.80	63.75	4.24	7.52	11.90	2.83	12.59	4.21	0.28	0.50	0.79	0.19	0.83
D. M.	7.04	1.28	56.17	5.60	10.48	14.65		13.07	3.95	0.39	0.74	1.03		0.92
D. S.	7.69	1.58	61.20	6.35	10.81	12.08	2.64	9.53	4.71	0.49	0.83	0.93	0.20	0.73
V. W.	6.45	1.20	54.66	4.10	11.33	12.95	2.98	13.94	3.53	0.26	0.73	0.84	0.20	0.90
H. J.	6.65	1.45	59.19	4.15	10.08	14.54		12.01	3.94	0.28	0.67	0.97		0.80
L. A.	6.65	1.40	58.55	5.39	11.15	13.01		11.90	3.89	0.36	0.74	0.87		0.79
M. K.	6.65	1.50	60.00	5.59	10.99	12.61		10.81	3.99	0.37	0.72	0.84		0.72
D. V.	7.86	1.34	57.32	4.61	11.25	12.33		14.50	4.50	0.36	0.88	0.97		1.14
Mean	6.88	1.44	59.14	5.04	10.04	13.43	2.68	12.34	4.11	0.35	0.71	0.93	0.18	0.84

* Measured only in descending column.

TABLE 3

Electrophoretic Mobilities of Serum Protein Fractions in the Aged Normal Group

(Mobility = 10^{-5} cm.^{2} V^{-1} sec.$^{-1}$)

Subjects	Albumin	Alpha 1	Alpha 2	Beta	Gamma 1*	Tot. Gamma
J. G.	−5.74	−4.82	−3.95	−2.93	−2.14	−1.35
C. G.	−5.92	−5.05	−4.07	−3.04		−1.41
R. H.	−5.95	−5.06	−4.00	−3.02	−2.41	−1.48
B. H.	−5.70	−4.96	−4.11	−2.81		−1.44
O. H.	−5.86	−5.08	−4.51	−2.98		−1.43
Ed. J.	−5.55	−4.70	−3.94	−2.81		−1.38
J. K.	−5.70	−4.83	−3.91	−2.80		−1.33
J. L.	−5.71	−4.90	−4.14	−2.83		−1.37
O. L.	−6.01	−5.17	−4.57	−3.07	−2.43	−1.44
H. M.	−5.78	−5.04	−3.91	−2.89		−1.32
S. S.	−6.24	−5.41	−4.39	−3.25	−2.38	−1.66
D. U.	−5.78	−4.98	−4.08	−2.88	−2.20	−1.33
F. V.	−5.25	−4.53	−3.64	−2.65	−1.96	−1.10
E. Y.	−5.86	−5.02	−4.01	−2.99		−1.52
Mean	−5.79	−4.97	−4.08	−2.93	−2.25	−1.40

* Measured only in descending column.

B. The appearance of the patterns in the younger normal group

The characteristics of the electrophoretic patterns in the younger normal group were similar to those in the aged normal group. The gamma-1 component was observed in 4 of the 9 patterns. The relative and absolute concentrations of the protein fractions are listed in Table 2 and the electrophoretic mobilities are shown in Table 4.

A comparison is made in Table 5 of the results of several studies by other investigators on normal human sera in NaV-HV buffer, ionic strength 0.1, pH 8.5 to 8.6. There is reasonably good agreement among the groups; slight variations in technique or even among groups of individuals may be expected. A comparison of our mobility determinations with those of Dole and Braun (6) shows a difference in the mobility of gamma globulin, but this may be a result of a difference in the method of determining the midpoint of its peak, which is usually relatively broad due to the chemical heterogeneity of this fraction.

TABLE 4

Electrophoretic Mobilities of Serum Protein Fractions of the Younger Normal Group

(Mobility = 10^{-5} cm.^{2} V^{-1} sec.$^{-1}$)

Subjects	Albumin	Alpha 1	Alpha 2	Beta	Gamma 1*	Tot. Gamma
J. K.	−5.75	−4.90	−4.09	−2.85	−2.24	−1.31
D. M.	−5.94	−5.06	−4.00	−2.92		−1.36
D. S.	−5.87	−5.00	−4.14	−3.04	−2.35	−1.40
H. J.	−5.73	−4.89	−3.98	−2.87		−1.41
L. A.	−5.94	−5.07	−3.96	−2.86		−1.19
M. K.	−5.95	−5.17	−4.17	−3.11		−1.46
D. V.	−5.98	−5.14	−4.03	−3.10		−1.52
Mean	−5.88	−5.03	−4.05	−2.96	−2.30	−1.38

TABLE 5

Serum Protein Patterns in Younger Normal Humans

Investigator	Albumin	Alpha 1	Alpha 2	Beta	Gamma
Relative Concentration of Serum Protein Fractions (Per Cent of Total)					
Dole and Braun (6)	60.3	4.6	7.2	12.1	11.0
Reiner, Fenichel and Stern (7)	56.8	7.2	8.7	12.8	14.4
Our series	59.14	5.04	10.04	13.43	12.34
Mobility = 10^{-5} cm.^{2} V^{-1} sec.$^{-1}$					
Dole and Braun (6)	−5.94	−5.07	−4.08	−2.83	−1.02
Our series	−5.88	−5.03	−4.05	−2.96	−1.38

C. Comparison of the aged normal group with the younger normal group

A comparison of the mean values of the aged normal group with those of the younger normal group is presented in Table 6 and reveals several differences: 1) there is a marked decrease in both the relative and absolute concentration of albumin in the aged group; 2) there is an increase in the relative concentration of alpha-1 globulin in the aged group (the slight increase in absolute concentration appears to be insignificant); 3) there is an increase in the percentage of alpha-2 globulin, which is reflected in a slight increase in absolute concentration; 4) there appears to be a moderate increase in the percentage of beta globulin, which is reflected in a less pronounced elevation in absolute concentration; and 5) the gamma globulin level appears to be elevated in the aged group, both in percentage and in total protein concentration. In general, the aged group as a whole shows a definite decrease in serum albumin content, whereas all serum globulin levels show an elevation which is most apparent in the beta and gamma fractions.

The total serum protein concentration in the aged group (6.08 grams per 100 ml.) is considerably lower than that in the younger group (6.88 grams per 100 ml.). The absolute decrease in serum albumin content is reflected in an albumin/globulin ratio of 0.88 in the older group as compared with a ratio of 1.44 in the younger group.

According to the mobility determinations presented in Tables 4 and 6, there are apparently no significant changes in mobility of the serum proteins in this series of aged normal people. The albumin component does show a tendency to migrate somewhat more slowly— -5.79×10^{-5} cm.^{2} V^{-1} sec.$^{-1}$ as compared with -5.88×10^{-5} cm.^{2} V^{-1} sec.$^{-1}$ in the younger normal series—but it is doubtful whether any significance can be attached to this observation, since electrophoretic mobility is a function of several incompletely understood variables.

It is noteworthy that there is a greater variation in the values for component percentage, absolute concentration, and mobility in the older group as indicated by larger standard deviations. A study of 15 normal human plasmas by Dole and Braun (6) reveals standard deviations comparable with those in our younger control group; studies by Reiner and coworkers (7) on 60 normal human sera show slightly higher standard deviations, but none of these studies reveals variations as large as those observed in our group of aged humans. Previous studies on geriatric patients have not shown the large ranges of values indicated in our series.

In several of the earlier studies of blood proteins in normal aged people, the separation of the serum or plasma protein fractions was accomplished by salting-out techniques. Olbrich (8) studied blood changes in a group of 37 male and 41 female normal aged persons and found a mean total serum protein concentration of 5.34 grams per 100 ml.; the mean serum albumin and globulin levels were 3.25 grams and 2.09 grams per 100 ml., respectively. These results indicated a decreased serum albumin content when compared with serum albumin and globulin values of 4.6 grams and 2.0 grams per 100 ml., respectively, in a control group of subjects less than 40 years of age. Bock (9) also noted a diminished serum albu-

TABLE 6

Comparison of Serum Protein Fractions and Electrophoretic Mobilities in the Younger Normal and Aged Normal Groups

(Mobility = 10^{-5}cm.^{2} v^{-1}sec.$^{-1}$) (All values negative.)

			Tot. Serum Protein (Gm./100 ml.)	A/G Ratio	Albumin	Alpha 1	Alpha 2	Beta	Gamma 1*	Tot. Gamma
Younger normal group	Per cent of total protein	Range	6.32–7.86	1.20–1.80	56.17–63.75	4.06–6.35	7.52–11.25	11.90–16.62	2.28–2.98	9.53–14.50
		Mean	6.88 ± 0.55	1.44 ± 0.18	59.14 ± 2.81	5.04 ± 0.89	10.04 ± 1.48	13.43 ± 1.86	(4)† 2.68	12.43 ± 1.63
	Grams per 100 ml.	Range			3.66–4.71	0.26–0.49	0.50–0.88	0.79–1.05	0.14–0.20	0.73–1.14
		Mean			4.15 ± 0.40	0.36 ± 0.08	0.71 ± 0.15	0.94 ± 0.10	0.18	0.87 ± 0.15
	Mobility (7)†	Range			5.73–5.98	4.89–5.17	3.96–4.17	2.85–3.11	2.24–2.35	1.19–1.52
		Mean			5.88 ± 0.10	5.03 ± 0.11	4.05 ± 0.08	2.96 ± 0.12	(2)† 2.30	1.38 ± 0.11
Aged normal group	Per cent of total protein	Range	4.80–7.43	0.56–1.33	35.91–57.04	3.60–11.49	8.39–16.22	9.55–22.22	1.60–6.53	4.83–30.19
		Mean	6.08 ± 0.67	0.88 ± 0.21	46.07 ± 5.83	6.30 ± 1.82	12.69 ± 2.14	17.33 ± 2.96	3.55 ± 1.29 (12)†	16.17 ± 4.52
	Grams per 100 ml.	Range			1.98–3.72	0.20–0.61	0.41–1.05	0.64–1.41	0.09–0.44	0.41–2.03
		Mean			2.80 ± 0.49	0.38 ± 0.10	0.77 ± 0.15	1.05 ± 0.19	0.20 ± 0.09	1.07 ± 0.35
	Mobility (14)†	Range			5.24–6.24	4.53–5.41	3.64–4.57	2.65–3.25	1.96–2.43 (6)†	1.19–1.66
		Mean			5.79 ± 0.23	4.95 ± 0.21	4.08 ± 0.26	2.93 ± 0.15	2.25 ± 0.19	1.40 ± 0.11

* Measured only in descending column.

† Number in series.

min concentration and a slightly elevated globulin level in his series of normal males and females whose ages ranged from 60 to 95 years; in this group the mean serum albumin concentration was 3.77 grams per 100 ml. and the value for serum globulin was 2.53 grams per 100 ml.. These studies are not directly comparable with experiments employing the electrophoretic method, since relatively large differences in percentage distribution of protein fractions may obtain if a given serum is analyzed by both methods. For example, Jager and associates (10) found that the chemical determination of serum albumin by precipitation with 21.5 per cent sodium sulfate resulted in values generally 10 to 15 per cent higher than those calculated by electrophoresis; on the other hand, both 26.0 per cent sodium sulfate and 26.9 per cent sodium sulfite yielded albumin values lower than those obtained by electrophoretic analysis.

Rafsky, Newman and Krieger (11) studied the plasma proteins of aged humans by electrophoresis in phosphate-NaCl buffer, pH 7.6, and found that the mean albumin percentage was lower than normal and the total globulin concentration was elevated, resulting in a lower A/G ratio. These findings are not strictly comparable with experiments employing Veronal buffers, since it is well established that alpha-1 globulin is not separated from albumin, and the gamma globulin gradient is not completely resolved from the delta and epsilon boundaries in phosphate buffer systems (12). Rafsky *et al.* (13) have, however, recently completed another study of the serum proteins in 31 normal aged humans employing the standard NaV-HV (Veronal) buffer system, ionic strength 0.1, pH 8.5–8.6, and the results confirmed their earlier observations. Except for their serum dilution factors of 1:1 or 1:1.5, their method is completely comparable with ours. A comparison of the two studies is listed in Table 7.

The percentage distribution of the serum protein fractions shows a similar pattern in both groups. Our results show somewhat less alpha-1 globulin and somewhat more alpha-2 globulin, but the other values are comparable. In terms of total protein concentration, the chief differences seem to be a lower value for albumin and alpha-1 globulin in our group. The mean total serum protein concentration appears to be lower in our series. The trends indicated in both groups

TABLE 7

Serum Protein Patterns in Aged Normal Humans

Investigator	Albumin	Alpha 1	Alpha 2	Beta	Gamma	A/G Ratio
Per Cent of Total Serum Protein						
Rafsky *et al.* (13)	48.6	8.5	10.2	16.7	15.9	0.97
Our series	46.07	6.30	12.69	17.33	16.17	0.88
Grams of Protein per 100 ml. Serum						
						Total
Rafsky *et al.* (13)	3.5	0.6	0.7	1.2	1.2	6.97
Our series	2.8	0.38	0.77	1.05	1.07	6.08

when compared with those in younger normal subjects are definitely in the same direction: the albumin/globulin ratio is lower, the albumin concentration is markedly lower, the beta globulin level is somewhat elevated, gamma globulin shows a definite tendency toward higher levels, and, although presently not of proven statistical significance, the alpha-1 and alpha-2 globulins are slightly elevated.

Goldbloom (14) recently analyzed the serum protein fractions in 10 normal aged patients 80 to 100 years of age, using the filter paper electrophoresis technique; the buffer system employed was diethyl barbiturate, pH 8.6, ionic strength 0.05. Although these experimental conditions are not directly comparable with those in the studies discussed here, the results indicated a similar trend in the series. Of the 10 patients, 4 showed a low concentration (per cent of total serum protein) of serum albumin and elevations in either gamma or beta globulin. The mean serum albumin concentration was 50.2 per cent in comparison with 61.0 per cent in a group of younger controls; the mean gamma globulin concentration was 23.4 per cent in the old group and 15.9 per cent in the control subjects. Absolute concentrations of the various protein fractions were not reported.

Not all investigators have observed disturbances in the serum or plasma protein fractions of the magnitude indicated in the foregoing reports. Parfentjev and Johnson (15) have completed an extensive study of the effect of aging on serum proteins in a group of 343 subjects varying in age from 20 to 90 years; the fractionation of serum proteins into albumin, globulin, euglobulin, and pseudoglobulin was accomplished by means of a turbidimetric procedure employing ammonium sulfate solutions. It was found that only in the age group 80–90 was there a significant percentage (17 per cent) of apparently healthy individuals who did not have a normal protein pattern; in these individuals there was a tendency toward lower albumin levels, increases in total globulin, and inversion of the albumin/globulin ratio. These workers suggested that, according to their study, an effect of age on the serum protein pattern was not apparent in the human being.

SERUM PROTEIN PATTERNS

1. Albumin

Hypoalbuminemia can be the result of several different factors: 1) inadequate protein intake, either by dietary deficiency or faulty utilization and absorption; 2) decreased ability of the body to synthesize albumin; 3) increased utilization of blood proteins, as in hyperthyroidism or pregnancy, or augmented protein catabolism incident to adrenocortical activation; and 4) loss from the blood in the urine or in exudates (16, 17). Definite tendencies toward hypoalbuminemia also occur in the presence of malignant conditions (15); several of the foregoing factors are probably involved under such circumstances.

Since the group of patients in this investigation was apparently free from pathologic conditions which would result in exudate formation or albuminuria, and since the diet on which they were maintained for at least two weeks prior to the study was adequate in protein, the observed hypoalbuminemia probably involves an imbalance between the rate of synthesis and the rate of tissue utiliza-

tion. In this group of patients, it could be reasonably assumed that the rate of tissue utilization of serum proteins would not be accelerated, since there were no obvious indications of rapid growth of new tissue or of gross endocrine imbalance. On the basis of our observations and those of the majority of other workers in this field, it would appear that the hypoalbuminemia associated with aging may be chiefly the result of a diminished rate of albumin synthesis. It must be emphasized, however, that the information on our subjects is not sufficient to rule out the possibility of a long-standing deficit in dietary protein, a condition which could possibly be reflected in the serum protein pattern regardless of the diet offered the subjects at least two weeks prior to and during this study. Some evidence of the time required for diet to affect serum protein concentration is indicated in the metabolism studies of Watkin and co-workers (18). Eight elderly men on ordinary diets were fed a high-protein diet (106 grams per day) for sixty-five days; there was an increase in total serum protein concentration from 7.16 grams to 7.72 grams per 100 ml. and an increase in albumin concentration from 4.55 grams to 5.38 grams per 100 ml. By rough estimation, according to these figures, it would require approximately eighty days to raise the serum albumin level by 1 gram per 100 ml. with the high-protein regimen; in all probability, it would take longer to restore a deficit of 1 gram of albumin per 100 ml., using an ordinary diet. The long-term relationship of diet to the serum protein pattern in the geriatric patient remains to be established.

If the hypoalbuminemia noted in this study does include as a factor a decreased rate of synthesis, it is necessary to consider several aspects of protein metabolism in attempting to arrive at an explanation. The experimental evidence of Knutti and associates (19) and Tarver *et al.* (20) indicates that the liver is the site of formation of all the fibrinogen, essentially all the albumin, and a large portion of the globulin fraction of plasma. The importance of the liver in the synthesis of albumin has been corroborated by the numerous clinical observations of varying degrees of hypoalbuminemia in cases of embarrassment of liver function associated with hepatitis and cirrhosis (16, 21, 22). However, hypoalbuminemia is certainly not limited to disease states involving liver dysfunction; in fact, it is considered by many to be a "common denominator" of almost every pathologic state, as a part of a general reaction of the body to injury and infection (17, 21). In the group of normal aged humans under consideration, it is important, therefore, to determine if the hypoalbuminemia is directly related to a waning capacity of the liver to perform its normal functions. Rafsky and Newman (23) carried out a series of liver function tests on a group of 50 normal individuals over 60 years of age and found that in 86 per cent at least one of the tests indicated liver dysfunction, in 26 per cent two of the tests showed abnormal function, and in 26 per cent four or more of the tests yielded abnormal results. The tests which they used included cephalin flocculation, bromsulphalein retention, hippuric-acid synthesis, and the determination of free and esterified cholesterol. Additional work is needed to verify these findings, but the evidence at hand would suggest that the observed hypoalbuminemia in the aged groups may be related, in part at least, to a decreased efficiency of liver function.

In our series of cases, liver function tests were made on all subjects; in practically all cases these included bromsulphalein retention, prothrombin time, cephalin-cholesterol flocculation or thymol turbidity, serum bilirubin (direct and indirect), and total and esterified cholesterol. In 1 case the results of two tests were borderline but were not considered sufficiently abnormal to eliminate the patient from the series. In 2 other cases cephalin flocculation readings of 3 plus (in forty-eight hours) were noted as the only abnormality; and since the results of all other tests in these cases were normal, these findings were not considered to be of great significance. Although the hepatic function of the patients in our series would appear to be essentially normal, as judged by the foregoing criteria, one may speculate whether a singular function of the liver, *i.e.*, protein synthesis, may be subnormal without disturbing other hepatic metabolic functions. This subject obviously requires further investigation.

In the earlier studies on blood proteins in the aged, Olbrich (8) maintained that his group received a diet similar to that of the general population. He suggested that the observed hypoalbuminemia may have been related to a decreased absorption of nutriments from the gut or to a decrease in protein formation. He also considered the possibility that the body's protein reserves may have been influenced by the previous nutritional history or that some disturbance existed in the "dynamic equilibrium" between dietary amino acids, plasma proteins and the body's labile reserve protein. Bock (9) also suggested that the hypoalbuminemia observed in his subjects may have been the result of either a depletion in protein reserves secondary to dietary inadequacies or a reduced "capacity" of plasma-forming organs.

Another important factor to consider when a "dynamic equilibrium" may be involved is the status of the endocrine system in the aged person. In recent years there has been considerable emphasis placed upon the function of the steroid sex hormones in promoting protein anabolism. In the geriatric patient one may expect diminished levels of gonadal hormones; since our group was composed largely of males (19 males, 2 females), the status of testicular secretion is of particular importance. Pearson and McGavack (24) recently demonstrated by chromatographic fractionation of urinary steroids that aged men excrete diminished quantities of androsterone, the principal metabolite of testosterone, and that the adrenal cortex apparently does not secrete androgen in compensation. It would seem that the deficiency of testicular secretion in the male should have some effect on the overall metabolism of protein, since he is still capable of responding to the protein anabolic effects of androgen. In the metabolic studies of Watkin *et al.* (18), the administration of stanolone, a synthetic androgen, to a group of males past 70 resulted in the retention of protoplasmic constituents (nitrogen, potassium and phosphorus) during administration of both high and low protein diets. It is of interest that they observed no significant changes in serum protein or albumin concentration; however, alterations in tissue hydration incident to fluid retention may have obscured the hormonal effects on blood proteins. Whatever the mechanisms whereby testosterone and other steroid hormones exert their protein anabolic effects, it would seem essential to consider

the changes in the endocrine status of geriatric patients as important factors in the evaluation of protein metabolism in general. It is interesting to speculate whether deficiencies in protein anabolic steroids can render the geriatric patient more susceptible to a metabolic deficiency of protein, even when receiving a diet considered to be "adequate."

It should be emphasized again that, although the metabolic factors discussed may be involved in the overall problem of protein metabolism and the status of the blood proteins, the effect of diet and long-standing protein deficiency may have overshadowed all other factors in our series and may have been the cause, not only of the wide range of serum protein values in our results but also of the variations in the findings of other workers in this field.

The ability of serum albumin to stabilize colloidal systems is an important feature of the colloidal gold test and the flocculation tests employed clinically in the evaluation of liver function; it is generally believed that qualitative changes in the albumin fraction result in colloidal instability as shown by an abnormal result (29, 30). In this respect, it is interesting to recall that none of the patients in our series showed abnormal results with flocculation tests (cephalin-cholesterol flocculation and/or thymol turbidity), except in 2 instances in which a cephalin flocculation reading of 3 plus (in forty-eight hours) was noted. This is no indication of what may have been expected from other tests of serum stability employing heavy-metal ions; however, it does illustrate that quantitative decreases in albumin concentration have little effect on the findings with the type of flocculation test employed in this study. If a hypoalbuminemia does accompany aging, it is possible that some lowering of serum stability may occur; nevertheless, it would appear that qualitative changes in the serum albumin level are of greater importance in this situation.

2. The alpha and beta globulins

Considerable experimental evidence has been obtained from electrophoretic, ultracentrifugal, and chemical fractionation studies to show that the alpha and beta globulin fractions comprise a heterogeneous group of lipoproteins, glycoproteins, and "simple" proteins, with small amounts of phospholipids, sterols, neutral fat, and other compounds migrating in the free state (16, 25).

In general, increases in alpha globulin accompany acute febrile diseases such as pneumonia, peritonitis and acute rheumatic fever, and are associated with inflammation or tissue destruction (16, 26). The alpha-2 fraction is increased generally in chronic disease states, such as tuberculosis and various types of malignancy, in which protracted wasting and destruction of tissue is involved; this finding usually parallels increased levels of serum glycoprotein (17).

Elevated beta globulins are almost always associated with the accumulation of lipids and lipoproteins in the blood, as seen in various disease states such as nephrosis, acute and chronic liver disease, malignant hypertension, and diabetes mellitus (27, 28). Unfortunately, there is considerable difference of opinion and variance in experimental results in the literature concerning the effects of aging upon serum lipid and lipoprotein levels; a complete discussion of this subject is

beyond the scope of this article. In view of the fact that the elevations in alpha and beta globulin levels in our series were not large, it would appear unwise to relate these findings to concomitant increases in serum lipid or glycoprotein levels without the actual isolation and characterization of the lipoproteins or glycoproteins by filter paper electrophoresis or ultracentrifugal analysis.

3. The gamma globulins

It is well known that most of the antibodies in human serum are contained in the gamma-globulin fraction. It is less well established whether this component, as observed in electrophoresis, represents a mixture of antibodies exclusively, or whether other functions may be assigned to these protein molecules. Cohn considers some of the protein molecules of this fraction to be "normal" gamma globulins and not true antibodies (27). The early work of Blix, Tiselius and Svensson (31) showed appreciable amounts of cholesterol and phospholipid in the gamma-globulin and albumin fractions in electrophoretically separated serum proteins, but later experiments employing ultracentrifugal and chemical fractionation methods indicated that both of these fractions were essentially lipid-free (25). Recently, however, some workers have reported that up to 3 per cent of total plasma cholesterol may be associated with the gamma-globulin fraction (32). The significance of this finding has not been determined.

A large body of information indicates that the reticuloendothelial system and the lymphatic tissue are the source of most of the gamma globulins (antibodies), although it is not definitely known which cells account for the direct synthesis of antibody protein (33, 34).

The gamma-globulin fraction is elevated in almost all cases of infections with various organisms, but such a response appears to be more a type of general body reaction than a simple increase in any specific antibody level, since the quantities of antibody sufficient to combat specific agents are often too small to be detected by electrophoresis (16). Evidence is accumulating to support the hypothesis that lymphocytes contain proteins which migrate with gamma globulin electrophoretically, and that the activation of the pituitary-adrenocortical system in situations of stress (infections) results in the dissolution of lymphocytes and the release of the protein material (35). However, it is still inconclusive whether these globulins represent antibodies in themselves, or whether they furnish structural proteins mobilized for protein synthesis in general. Great increases in serum gamma-globulin levels occur in infectious diseases which induce marked inflammatory responses in the reticuloendothelial system, such as kala azar, lymphopathia venereum, syphilis, granuloma inguinale, leprosy and tuberculosis; this illustrates the striking relationship between augmented levels of gamma globulin and the hyperactivity of the reticuloendothelial system in response to an antigenic stimulus (16).

Liver diseases, especially hepatitis and cirrhosis, are also characteristically associated with elevated levels of gamma globulin (16, 21, 22, 36). Large increases are also generally consistent findings in sarcoidosis, lupus erythematosis, rheumatoid arthritis, and periarteritis nodosa (17).

With this diverse array of possibilities, it is almost impossible to attach significance to the increase in gamma globulin content of sera from normal aged humans. Parfentjev (37) studied the effects of aging in dogs and chickens and noted that the main alteration in blood proteins was a gradual increase in globulin levels; he suggested that these changes were related to the continuous contact of the animals with infectious organisms and a resulting hyperimmunization phenomenon. It is possible that clinically undetected low-grade infections in geriatric patients may account, in part at least, for the elevated levels of gamma globulin. It is also possible that the elevation of all the globulin fractions (including gamma) may be a response of the body to the low albumin levels, since Gray and Barron (36), along with other investigators, postulate that the body attempts to maintain the osmotic pressure of plasma by an increased synthesis of globulin in the face of hypoalbuminemia. However, Gutman (16) does not believe that such a compensatory mechanism is probable, since the osmotic pressure of the globulins, and especially that of gamma globulin, is very low compared with that of albumin.

Deutsch, Alberty and Gosting (38) were among the first to report a globulin showing an electrophoretic mobility slightly greater than that of ordinary gamma globulin. They noted that after removal of fibrinogen and gamma globulin from plasma by precipitation with ethanol, a portion of the gamma globulin remained which they designated as gamma-1 globulin; this fraction migrated with the approximate velocity of fibrinogen, namely, -2.14×10^{-5} cm.^{2} V^{-1} sec.$^{-1}$ (6). Immunologic studies revealed that a major portion of typhoid "O" agglutinin and a portion of the hemagglutinins of plasma were associated with the gamma-1 fraction. However, it was suggested that a portion of this fraction may be a lysis product of fibrinogen. The gamma-1 fraction appeared to comprise from 2 to 3 per cent of normal plasma proteins in their series.

The importance of recognizing the presence of gamma-1 globulin was later shown in studies of chronic liver ailments by electrophoretic analysis of plasma and serum proteins (39). Although chemical techniques indicated some decrease in fibrinogen levels, electrophoretic analysis of plasma showed an elevation of the "fibrinogen" peak, and this peak was not obliterated in the analysis of serum. The serum "fibrinogen" peak apparently represented the gamma-1 globulin fraction and, therefore, the correct evaluation of the fibrinogen peak in plasma was obscured. In normal sera, the gamma-1 fraction accounted for 2.4 per cent, in acute hepatitis 3.9 per cent, in obstructive jaundice 4.1 per cent, and in cirrhosis 7.0 per cent of the total serum protein. These findings emphasize the need for caution in interpreting plasma fibrinogen values obtained by the method of electrophoresis.

In the light of the foregoing discussion, the observation of an increase in gamma-1 globulin concentration from 2.7 per cent in the younger normal group to 3.6 per cent in the aged normal group would tend further to suggest some impairment of liver function; but when compared on the basis of absolute concentration, the increase from 0.18 gram to 0.20 gram per 100 ml. would not seem significant. Moreover, gamma-1 globulin cannot be demonstrated in measurable

amounts in all sera of either the younger or the aged group. Further studies on the nature of this interesting fraction are necessary in order to determine whether it represents some residual fibrinogen, a lysis product of fibrinogen, or a true segment of antibody protein, before any significance can be attached to its presence.

SUMMARY

The electrophoretic data presented in this study, together with that of other workers in this field, indicate a relative and absolute decrease in albumin content of serum from normal aged humans. Although conclusive evidence is not available, this observation may indicate a diminished rate of albumin synthesis secondary to a progressive decrease in efficiency of liver function associated with senility. The hypoalbuminemia, however, may be a reflection of a prolonged deficiency of dietary protein; there is no evidence to eliminate this possibility and further investigation is necessary to evaluate this factor. The possible relationship of decreased gonadal secretion accompanying senility and hypoalbuminemia has been briefly discussed.

All the globulin fractions appear to be elevated in both relative and absolute concentration in aged humans, with the most significant increases appearing in the beta and gamma globulin components. The significance of these changes has been discussed.

REFERENCES

1. Lippman, R. W., and Banovitz, J.: The influence of protein concentration upon electrophoretic mobility of serum proteins, *J. Biol. Chem.* **199:** 451–456, 1952.
2. Perlmann, G. E., and Kaufman, D.: The effect of ionic strength and protein concentration in the electrophoretic analysis of human plasma, *J. Am. Chem. Soc.* **67:** 639–641, 1945.
3. Tiselius, A., and Kabat, E. A.: An electrophoretic study of immune sera and purified antibody preparations, *J. Exper. Med.* **69:** 119–131, 1939.
4. Stern, K. G., and Reiner, M.: Boundary artifacts and anomalies in electrophoresis, *J. Electrochem. Soc.* **97:** 213–218, 1950.
5. Levin, R., and Brauer, R. N.: The biuret reaction for the determination of protein —An improved reagent and application, *J. Lab. & Clin. Med.* **38:** 474–480, 1951.
6. Dole, V. P., and Braun, E.: Electrophoretic patterns of normal plasma, *J. Clin. Invest.* **23:** 708–713, 1944.
7. Reiner, M.; Fenichel, R. L., and Stern, K. G.: Electrophoretic studies on the protein distribution in normal human serum, *Acta haemat.* **3:** 202–210, 1950.
8. Olbrich, O.: Blood changes in the aged. III. Plasma proteins, *Edinburgh M. J.* **55:** 100–115, 1948.
9. Bock, J.: Serum protein fractions in normal old individuals, *J. Gerontol.* **3:** 119–123, 1948.
10. Jager, B. V.; Schwartz, T. G.; Smith, E. L.; Nickerson, M., and Brown, D. M.: Comparative electrophoretic and chemical estimation of human serum albumin; an evaluation of six methods, *J. Lab. & Clin. Med.* **35:** 76–86, 1950.
11. Rafsky, H. A.; Newman, B., and Krieger, C. I.: An electrophoretic analysis of the plasma proteins in the aged, *Am. J. M. Sc.* **217:** 206–210, 1949.
12. Longsworth, L. G.: Recent advances in the study of proteins by electrophoresis, *Chem. Rev.* **30:** 323–340, 1942.

13. Rafsky, H. A.; Brill, A. A.; Stern, K. G., and Corey, H.: Electrophoretic studies on the serum of normal aged individuals, *Am. J. M. Sc.* **224:** 522–528, 1952.
14. Goldbloom, A. A.: New clinical and laboratory studies in the aged. V. Lipidogram by paper electrophoresis in normal patients 80–100 years of age, *Am. J. Digest. Dis.* **22:** 51–58, 1955.
15. Parfentjev, I. A., and Johnson, M. L.: The plasma protein pattern and its significance in geriatrics and cancer diagnosis, *Geriatrics* **10:** 232–238, 1955.
16. Gutman, A. B.: The plasma proteins in health and disease, *Adv. in Protein Chem.* **4:** 156–250, 1948.
17. Luetscher, J. A.: Biological and medical applications of electrophoresis, *Physiol. Rev.* **27:** 621–642, 1947.
18. Watkin, D. M.; Parsons, J. M.; Yiengst, M. J., and Shock, N. W.: Metabolism in the aged. The effect of stanolone on the retention of nitrogen, potassium, phosphorus, and calcium and on the urinary excretion of 17-keto, 11-oxy, and 17-hydroxy steroids in eight elderly men on high and low protein diets, *J. Gerontol.* **10:** 268–287, 1955.
19. Knutti, R. E.; Erickson, C. C.; Madden, S. D.; Rekers, P. E., and Whipple, G. H.: Liver function and blood plasma protein formation, *J. Exper. Med.* **65:** 455–467, 1937.
20. Tarver, H., and Reinhardt, W. O.: Methionine labeled with radioactive sulfur as an indicator of protein formation in the hepatectomized dog, *J. Biol. Chem.* **167:** 395–400, 1947.
21. Young, E. G., and Webber, R. V.: On the origin of human plasma proteins. Electrophoretic analysis in selected pathological states, *Canad. J. M. Sc.* **31:** 45–63, 1953.
22. Popper, H.; Bean, W. B.; de la Huerga, J.; Franklin, M.; Tsumagari, Y.; Routh, J. I., and Steigmann, F.: Electrophoretic serum protein fractions in hepatobiliary disease, *Gastroenterology* **17:** 138–162, 1951.
23. Rafsky, H. A., and Newman, B.: Liver function tests in the aged, *Am. J. Digest. Dis.* **10:** 66–69, 1943.
24. Pearson, S., and McGavack, T. H.: Effect of age upon the relative gonadal adrenocortical activity of the male, *J. Gerontol.* **10:** 312–314, 1955.
25. Edsall, J. T.: The plasma proteins and their fractionation, *Adv. in Protein Chem.* **3:** 383–479, 1947.
26. Longsworth, L. G.; Shedlovsky, T., and MacInnes, D. A.: Electrophoretic patterns of normal and pathological human blood serum and plasma, *J. Exper. Med.* **70:** 399–413, 1939.
27. Stern, K. G., and Reiner, M.: Electrophoresis in medicine, *Yale J. Biol. & Med.* **19:** 67–99, 1946.
28. Lewis, L. A., and Page, I. H.: Electrophoretic and ultracentrifugal analysis of serum lipoproteins of normal, nephrotic and hypertensive persons, *Circulation* **7:** 707–717, 1953.
29. Kabat, E. E.; Hanger, F. M.; Moore, D. H., and Landow, H.: Relation of cephalin flocculation and colloidal-gold reactions to serum proteins, *J. Clin. Invest.* **22:** 563–568, 1943.
30. Ham, T. H.: A Syllabus of Laboratory Examinations in Clinical Diagnosis. Cambridge, Mass., Harvard Univ. Press, 1952, p. 388.
31. Blix, G.; Tiselius, A., and Svensson, H.: Lipids and polysaccharides in electrophoretically separated blood serum proteins, *J. Biol. Chem.* **137:** 485–494, 1941.
32. Surgenor, D. M.: Extracellular lipoproteins, *in* Symposium on Atherosclerosis, National Academy of Sciences. Washington, D. C., National Research Council, 1954, Part V, p. 203.
33. Harris, T. N., and Harris, S.: Biological and technical factors in the demonstration of antibody production by lymphatic tissue, *J. Immunol.* **64:** 45–56, 1950.
34. Hayes, S. P., and Dougherty, T. F.: Studies on local antibody production, *J. Immunol.* **73:** 95–97, 1954.

35. Frieden, J., and White, A.: Studies of electrophoretic serum protein patterns in subjects treated with pituitary, adrenal cortical hormones, nitrogen mustard, or x-radiation, *Yale J. Biol. & Med.* **22:** 394–406, 1950.
36. Gray, S. J., and Barron, E. S. G.: The electrophoretic analysis of the serum proteins in diseases of the liver, *J. Clin. Invest.* **22:** 191–200, 1943.
37. Parfentjev, I. A.: Changes in serum proteins during aging in humans and animals, *J. Gerontol.* **9:** 363–364, 1954.
38. Deutsch, H. F.; Alberty, R. A., and Gosting, L. J.: Biophysical studies of blood plasma proteins. IV. Separation and purification of a new globulin from normal human plasma, *J. Biol. Chem.* **165:** 21–35, 1946.
39. Franklin, M.; Popper, H.; de la Huerga, J.; Bean, W. B.; Steigmann, F.; Routh, J. I., and Budde, M. S.: Comparison of the electrophoretic pattern of serum and plasma in liver disease with special reference to the gamma globulin fraction, *J. Lab. & Clin. Med.* **34:** 1600–1601, 1949.

HOST-TUMOR ANTAGONISM

I. Evidence for the Existence of "Tumor Immunity"

LOUIS PELNER, M.D.*

Swedish Hospital in Brooklyn, Brooklyn, N. Y.

Cancer may be defined as a new growth of cells, autonomous in nature and serving no useful function (1). The fact that no useful function is served distinguishes cancer from reparative processes. We may well ask if cancer is really autonomous. It is now known that certain cancers are hormone-dependent; although, once started, they seem to be independent of the exciting cause, their growth can be controlled in some measure. Another method of control may some day be proved, namely, tumor immunity. This method appears to be one of the fruitful leads at the present time.

The older literature is replete with many case histories of cases of cancer that were "spontaneously" cured, and even more so, of patients with hopeless cancer who lived a phenomenally long time. In 1909 Handley (2), the famous English physician, stated unequivocally: "I hope to show that, as I have stated elsewhere, the progress of cancer is normally accompanied by retrogressive or curative processes; that the recorded cases of natural repair in cancer, far from being anomalous and exceptional, merely illustrates more strikingly than usual the natural laws which govern every case of the disease. The order of Nature admits of no real anomalies, and it is often brought to light by the close study of apparent exceptions."

It has been known since the beginning of the century that some sort of immunity exists to transplantable tumors. Although the presence of antibodies seemed probable as the basis of this immunity in some experimental animals and in certain humans with cancer, several of the early workers could not find them. Ehrlich and his co-workers (3) finally concluded that the immunity was of the athreptic type, that is, it was due to the absence of specific nutritive substances upon which the growth was supposed to depend. This view is no longer held.

Several of the early authors reported occasional spontaneous regression of experimentally inoculated tumors in mice. However, the most important early article on the subject was written by Gaylord and Clowes (4) in 1906. They introduced a special charting system, so that each experimental member could be followed closely. In 711 mice that were inoculated with the Jensen mouse sarcoma, there were 445 fatal tumors, 400 of which attained a considerable size; 101 mice showed unquestionable spontaneous regressions.

These workers noted that a mouse that recovered from carcinoma could not be successfully inoculated again within a certain period. This immunity could not always be successfully maintained in some of the animals, since some tumors remained stationary or regressed but later overcame the host resistance and killed

* F.A.C.A. Attending Physician, Swedish Hospital.

the animal. Gaylord and Clowes felt that the evidence of retrogression at the margins of growing tumors was due to insufficient activity of the immune forces. They could reduce the number of successful takes, if the tumor material was mixed with the blood of the recovered mice.

Weil (5) was at first unable to demonstrate antibodies against experimental tumors, even by attempting to induce anaphylactic reactions. Normal guinea pigs were given intraperitoneally various amounts of plasma from rats with regressed tumors and two days later they were given intravenously an extract of rat sarcoma. He could not induce anaphylaxis in these animals. Weil concluded that it was therefore impossible to demonstrate the presence of immune substances in resistant rats by the method of anaphylaxis.

In his last paper on the serum factor in tumor immunity, Weil (6) reversed his former position. He combined immune serum with minced tumor and injected the mixture into the jugular vein and noted the number of pulmonary tumors that had developed. Immune serum reduced the number of pulmonary "takes" to one third the number found when tumor tissue alone was used.

Lumsden (7) believed that he could demonstrate anti-malignant cell antibodies. He was able to produce antiserum in animals by injecting heterologous tumor tissues. The immune properties of this serum could only be demonstrated in tissue cultures, because the serum could not reach the malignant cells in effective amounts in the intact animal.

Lumsden inoculated the Jensen rat sarcoma into both feet of rats, and after the growth of the tumors, he applied a rubber band to an ankle so as to occlude the blood vessels; he then injected antiserum into this tumor. Invariably, the tumors in the treated foot regressed rapidly, and in almost all the animals regression of the untreated tumor occurred later. Lumsden felt that the regression in the untreated foot was not spontaneous, but was induced by the production of immune substances. Among 50 control animals, the tumors regressed spontaneously in 5 cases. It is to be noted that all the cured animals were found to be immune to a subsequent challenge graft even after six months.

Lumsden felt that the slow regression of a tumor was essential in order to effect a cure and evoke an immunity. Absorption of antigenic material from the dying tumor acted like a vaccine and induced an active immunity in the animal against the tumor concerned. Similar experiments have recently been performed by others, with confirmation of his results.

Lumsden believed that the antiserum method was a relatively ineffective way to treat tumors, and that the production of an active immunity would probably be more effective. He noted that the inoculation of normal tissues, after the method of Bashford (8) would produce a slight immunity to subsequent challenge grafts. Because he felt that immunity was evoked only when tumor cells grew actively for a time in the host and then regressed, he tried to cure implanted tumors already growing in animals. This method he called autovaccination.

Lumsden injected 1 per cent formalin into growing Jensen rat tumors daily until the tumors ceased to grow. Regression thereafter started in about five days. Of 43 animals cured in this manner, 40 were immune to subsequent challenge inoculation.

Lumsden felt that autovaccination aided the natural protective mechanism possessed by each animal. He stated that the rare, but well authenticated cases of spontaneous recovery in human cancers justified the hope that the body resists the invasion of its tissues by malignant cells by a comparable mechanism to that evoked by transplanted tumors.

Although it had been known that immunity to transplanted tumors occasionally could be induced by inoculation of tumor tissue and even temporarily by normal tissues (8), it was also known that the inoculations themselves could produce tumors.

In 1910, Contamin (9) noted that in mice he could produce immunity to transplanted tumors by first inoculating the animals with tumor material treated with x-rays *in vitro*. These observations were extended by Wedd, Morson and Russ (10). Their animals were protected, and the irradiated tumor cells did not develop into a tumor. The amount of radiation used on the tumor tissue was twice the amount that would prevent the development of tumors with the irradiated tissues in normal rats.

As a result of these experiments, Kellock, Chambers and Russ (11) attempted to immunize humans against their own neoplasms, using an amount of radiation on the tumor graft that they felt would retain immunizing power, but would abolish growth. Twelve patients were so treated, by the removal of their tumors and by the injection of part of this irradiated cancer material. Five of the patients had died, but the remainder were in comparatively good health at the time of publication of their article. Although the results in these patients could not be considered spectacular, the experiment seemed to contain the germ of a good idea.

However, these experiments were contraverted by Wood (12) and by Wood and Prigosen (13), who showed that an inoculation of tumor cells devitalized by x-ray or radium could not prevent successful inoculation with a vigorous tumor. Finally, Wood pointed to a human case, in which the inoculation of irradiated human material was followed by extensive metastases.

Russ and his colleagues, and even Wood and Prigosen, could not measure the dose of radiation used on their tumor material, so that results could not be duplicated by different groups. Goldfeder (14) repeated the animal research in 1940–1942, but she had the advantage of being able to measure the radiation given to the grafts in precise roentgen units. A graft given 4,000–5,000 units of irradiation will not cause a tumor to grow, but will subsequently protect the animal against a transplanted tumor of the same type. A dose of 60,000 units will not protect the animal against a subsequent challenge inoculation.

Stone, Curtis and Brewer (15) also attempted to evoke resistance to cancer in humans. In an experiment, in which the cancer cells were treated by freezing to −50°C. for eight days, only 10 per cent of successful inoculations occurred in susceptible mice. With natural tumor, successful inoculation occurred in 95 per cent of the mice.

On the basis of these experiments, Stone tried the method in 4 human cases—in 1 for only a very brief period before publication. All were stated to be extremely unfavorable breast cancer patients. In 3 of the cases, frozen material

from the patient's own carcinoma was implanted, and in the fourth case, material from another patient was used. Two of the patients died within several months without any apparent change up to the time of death. The third patient fared better, but sixteen months after implantation, a small nodule of tumor was noted; this was excised, and the patient is alive three and a half years after operation. It would, therefore, be hazardous to treat patients in this fashion unless the prospect of orthodox treatment would be expected to give a very poor result.

A great many modern observers agree that antibody production by the host after tumor inoculation does occur, but not after all inoculations, and not in all animals, even of the same strain. The reason for this lack of uniformity is unknown. It may suffice to review several of the most modern articles.

Hoyle (16) reported that alcoholic extracts of some mouse tumors yielded positive results in complement fixation tests with serum of mice bearing these tumors. These antigens are probably lipoid and may be identical for several tumors. The antigen was not present in normal mouse tissues, and the antibody was not present in the serum of normal mice. Hoyle felt that the reason why antibody could not be found in the serum of all the inoculated mice, was that they did not live long enough to develop it. Some of the animals were moribund four weeks after grafting; the animals surviving for longer periods, showed greater incidence of antibody content.

Fink (17) and her co-workers demonstrated antibody in strain BALB/C mice to homologous tumor S621 by the use of two techniques—anaphylaxis, and tumor regression. Mice of this strain were given four intra-abdominal injections of lyophilized tumor and subsequently were shocked by intravenous injections of tumor suspension into the tail vein. Symptoms of anaphylaxis occurred in a large proportion of the sensitized mice, but not in the non-sensitized controls. Shock was not observed when extracts of other tumors were given intravenously, which attests to the specificity of the reaction.

Because of the many unknown factors inherent in the tumor-host relationship, the experimental approach to the demonstration of antibody formation to malignant tissue is difficult. We do not know which portion of the tumor cell differs from normal tissue—and a difference must be present for the cell to be antigenic. The *in vivo* method of demonstrating antibody is therefore warranted. Fink and her co-workers believe that a quantitative relationship exists between the amount of antibody necessary to induce anaphylaxis and the amount necessary to induce tumor regression.

In recent years, great interest has been shown in the methods of inducing tumor immunity demonstrated by Lewis and Aptekman and their associates (18). In an early experiment, a concentrate of an alcoholic extract of a rat sarcoma was injected into a transplanted sarcoma in an homologous inbred strain of rats. This caused a rapid lysis of the tumor, followed by sloughing and complete healing. After several weeks or months, the recovered rats were found refractory to challenge grafts of the homologous sarcoma.

Later these workers produced a sarcoma in inbred rats by injection of methylcholanthrene in mineral oil. These sarcomas were 100 per cent transplantable. An

alcoholic extract was made by the method previously mentioned, and this was injected into rapidly growing tumors. After lysis had occurred in these tumors, the rats were challenged with grafts of the same tumors. The immunity was still present ten to twelve months later.

Lewis and Aptekman attempted to prepare a vaccine from atrophied sarcoma tissue, which was produced by tying off the blood vessels of the tumor and sewing it into a permanent pocket. The tumors degenerated into semi-solid material, and 0.5 cc. of this material was injected into susceptible rats. Three weeks to two months later, the treated rats were challenged by grafts of viable homologous sarcoma tissue. The tumor did not grow in any of the vaccinated rats.

From this brilliant work, it may be concluded that the optimum conditions for the development of immunity are (19):

1. The tumor must actually grow in the host.
2. The tumor must die in the host.
3. The tumor tissue must degenerate under conditions that permit slow absorption of the degeneration products.

Recently Graham and Graham (20) were able to demonstrate antibodies in human cases of carcinoma by the complement fixation technique, using the patient's tumor as antigen and the patient's serum as the source of antibodies. Twelve of 48 patients showed significant titers ranging from 1:16 to 1:128. The authors found that those in whom antibodies had developed showed lesions that were completely removable or were capable of responding satisfactorily to radiation therapy. Six patients showed a significant titer after removal of the tumor. In eighteen of the 36 patients in whom antibodies could not be demonstrated, the outlook on clinical grounds was unfavorable. The serum from 25 normal persons gave only one complement fixation reaction with one of the tumors.

The Grahams believe that a patient with a widespread unchecked malignancy is less likely to have demonstrable antibodies. If the antibody were produced, it probably would be immediately fixed by the tumor. In 1 patient, a low preoperative titer became a very high postoperative titer which later gradually subsided. Two patients had no demonstrable antibodies before operation, but showed a definite titer after operation; this suggested to the Grahams that the antibodies were originally fixed by the tumor. Because of such results, these authors feel that the virulence of the tumor is less important than the resistance of the host, and that therapy should be governed accordingly.

Are we justified in judging the host resistance in all cancer patients by the disease as we often observe it in many of the far advanced clinical cases? The patient with spreading cancer may well represent a failure of the immune mechanism. By the same token, it is possible that if the immune mechanism be sufficiently active, cancer may never reach the clinical stage.

REFERENCES

1. Steiner, P. E.: The Nature of Cancer. Canadian Cancer Conference. New York, Academic Press, Inc., 1955.

2. HANDLEY, W. S.: A lecture on the natural cause of cancer, *Brit. M. J.* **1:** 582, 1909.
3. EHRLICH, P., AND APOLANT, H.: Beobachtungen über maligne Mausetumoren, *Berl. klin. Wchnschr.* **42:** 871, 1905.
EHRLICH, P.: Experimentelle Carcinomstudien au Mausen, *Arb. a.d. konigl. Inst. f. exper. Therap. z. Frankfurt A.M.* **1:** 77, 1906.
APOLANT, H.: The question of athrepsia, *J. Exper. Med.* **14:** 316,1911.
4. GAYLORD, H. B., AND CLOWES, G. H. A.: On spontaneous cure of cancer, *Surg., Gynec. & Obst.* **2:** 633, 1906.
5. WEIL, R.: On tumor immunity in rats, *Proc. Soc. Exper. Biol. & Med.* **9:** 32, 1911–1912.
WEIL, R.: A study of the blood of rats recovered from implanted sarcoma, *J. Exper. Med.* **18:** 390, 1913.
WEIL, R.: Passive immunization against rat sarcoma: immune substances in the blood of rats recovered from tumor, *J.A.M.A.* **60:** 2020, 1913.
WEIL, R.: On immune substances in the blood of rats recovered from tumors, *Ztschr. f. Krebsforsch.* **13:** 538, 1913.
6. WEIL, R.: A study of the serum factors in tumor immunity, *J. Cancer Res.* **1:** 389, 1916.
7. LUMSDEN, T.: Observations on cancer cells in vitro, *Brit. M. J.* **2:** 1003, 1924.
LUMSDEN, T.: Tumor immunity, *Am. J. Cancer*, **15:** 563, 1931.
LUMSDEN, T.: Immunity to implanted tumors, *Lancet* **1:** 258, 1927.
LUMSDEN, T.: Cancer and adrenalin, *Lancet* **2:** 733, 1927.
LUMSDEN, T., AND STEPHENS, J. G.: Note on the treatment of Jensen's rat sarcoma by antiserum and adrenalin, *Lancet* **2:** 375, 1927.
8. BASHFORD, E. F.: The bearing of immunity reactions on the nature of cancer, *in* Tr. XVII Internat. Cong. Med., London, 1913 (Subsection IIIa, p. 29).
9. CONTAMIN, A.: Immunisation contre le cancer de la souris inoculée avec des tumeurs modifiées par les rayons X, *Compt. rend. Acad. d. sc.* **150:** 128, 1910.
10. WEDD, B. H.; MORSON, H. C., AND RUSS, S.: On the immunity conferred on mice by radium-irradiated mouse carcinoma, *J. Path. & Bact.* **18:** 566, 1913–14.
11. KELLOCK, T. H.; CHAMBERS, H., AND RUSS, S.: An attempt to procure immunity to malignant disease in man, *Lancet* **1:** 217, 1922.
12. WOOD, F. C.: Discussion, *J. Cancer Res.* **4:** 57, 1919.
WOOD, F. C.: Immunity in cancer, *J.A.M.A.* **85:** 1039, 1925.
13. WOOD, F. C., AND PRIGOSEN, R. E.: No immunity produced by inoculating irradiated tumor tissue, *J. Cancer Res.* **9:** 287, 1925.
14. GOLDFEDER, A.: Effects produced by different dosage rates of x-radiation upon growth factors of mouse sarcoma 180, *Radiology* **37:** 705, 1941.
GOLDFEDER, A.: Effects produced by different dosage rates of x-ray radiation on the proliferation of various tissues grown in vitro, *Radiology* **35:** 210, 1940.
GOLDFEDER, A.: Relation between radiation effects and cell viability as indicated by induced resistance to transplanted tumors, *Radiology* **39:** 427, 1942.
15. STONE, H. B.; CURTIS, R. M., AND BREWER, J. H.: Can resistance to cancer be induced? *Ann. Surg.* **134:** 519, 1951.
16. HOYLE, L.: A lipoidal antigen produced by certain malignant tumors of the mouse, *Am. J. Cancer* **39:** 224, 1940.
17. FINK, M. A.; SNELL, G. D., AND KELTON, D.: Demonstration of antibody in strain BALB/C mice to homologous tumor S621, by the use of two techniques—anaphylaxis and tumor regression, *Cancer Res.* **13:** 666, 1953.
18. APTEKMAN, P. M.; LEWIS, M. R., AND KING, H. D.: A method of producing in inbred albino rats a high percentage of immunity from tumors native in their strain, *J. Immunol.* **52:** 77, 1946.
APTEKMAN, P. M.; LEWIS, M. R., AND KING, H. D.: Tumor immunity induced in rats by subcutaneous injection of tumor extract, *J. Immunol.* **63:** 435, 1949.
LEWIS, M. R.; APTEKMAN, P. M., AND KING, H. D.: Inactivation of malignant tissue in tumor-immune rats, *J. Immunol.* **61:** 321, 1949.

LEWIS, M. R.; AND APTEKMAN, P. M.: Antigenicity of sarcomata undergoing atrophy in rats, *J. Immunol.* **67:** 193, 1951.

APTEKMAN, P. M., AND LEWIS, M. R.: Progressive tumor resistance in successive generations of inbred immunized rats, *Science* **114:** 577, 1951.

APTEKMAN, P. M., AND LEWIS, M. R.: Evidence of resistance to tumor graft in early stages of induced oncolysis, *J. Immunol.* **66:** 361, 1951.

LEWIS, M. R., AND APTEKMAN, P. M.: Atrophy of tumors caused by strangulation and accompanied by development of tumor immunity in rats, *Cancer* **5:** 411, 1952.

19. RHOADS, J. E.: Discussion of (15).
20. GRAHAM, J. B., AND GRAHAM, R. M.: Antibodies elicited by cancer in patients, *Cancer* **8:** 409, 1955.

NURSE-PATIENT RELATIONSHIPS

BEATRIX COBB, PH.D.*

in professional collaboration with

M. CATHERINE ASHER, R.N., MABEL EMBREY, R.N., CATHERINE TOWEY, R.N., ESTELLE CHAMPAGNE, R.N. AND MARIAN METCALF, R.N.

Department of Medicine, The University of Texas M. D. Anderson Hospital and Tumor Institute, Houston, Texas

How does the patient feel about nurse-patient relationships? What are his expressed needs and the expectations from his nurse in the hospital setting? There has been much generalization as to the importance of nurse-patient relationships with respect to the person who is ill and hospitalized. A few excellent experimental studies, approaching the subject of interpersonal relations from a nurse-training angle, have appeared in the literature (1, 2). No systematic investigation was found reporting a study of the patient's reactions to the nurse and his desires in terms of an "ideal" nurse. Such a study would seem of value in theory and practice for both nurse-training and service programs.

TECHNIQUES AND METHOD OF INVESTIGATION

This article reports an investigation of the needs and expectations in the nurse-patient relationships as elicited from 50 patients hospitalized for a serious chronic disease—cancer.

Two problems were inherent in the choice of technique to be utilized in the nurse-patient relationships investigation. First, it must be rather simple. Second, it must probe into the three areas of patient response: 1) feelings about nurses in general, 2) feelings about the nurses in the specific setting, and 3) his "ideal" nurse. After some consideration, a variation of the Moral Ideologies Test was chosen.[1] This technique was designed to elicit responses from the patient concerning his feelings in the three areas, with as little structuring of response as possible: it was labelled a "Hospital Ideologies Technique." A copy is shown in Table 1.

The first category—having to do with routine nursing skills and phrases related to the physical comfort of the patient—was listed as "The Science of Nursing." The second category—having to do with psychologic skills and intangible qualities of the nurse bearing upon the emotional comfort of the patient—was listed as "The Art of Nursing." The third category—composed of a small number of items not falling under either of the two major divisions—was listed as "Miscellaneous." Quantitative analyses of the responses in the three areas as tabulated in the defined categories are shown in Tables 2–5.

An evaluation of the category designated as "The Art of Nursing" revealed

* Head, Medical Psychology Section.

[1] Originated by Alex Bavelus and employed in studies of Indian tribes by the personnel of the Committee On Human Development of The University of Chicago.

TABLE 1

Hospital Ideologies Technique

Eight things that I think a nurse should do, think, or feel:
1.
2.
3.
4.
5.
6.
7.
8.

Eight things that I think a nurse should not do, think, or feel:
1.
2.
3.
4.
5.
6.
7.
8.

My ideal nurse is like this:

The thing I like *best* about the nurses here is:

The thing I like *least* about the nurses here is:

TABLE 2

Categories of Responses to Hospital Ideologies Technique by Cancer Patients, with Respect to Nurses

Hospital Ideology	The Science of Nursing	The Art of Nursing	Total
Positive, "Good"	88	247	335
Negative, "Bad"	44	178	222
Totals	132	425	557

interesting subdivisions. Generally, "social personality" of the nurse and "communication" seemed to be the major concerns of the patients. Under social personality were listed all adjectives describing the nurse as a person. Communication included both verbal and non-verbal interactions between nurse and patient. The verbal had to do with a two-way communication of talking and listening, and the non-verbal consisted of feeling tones and attitudes which the patients seemed to interpret either as "good" or "bad." Table 3 epitomizes this subdivision according to meaning. Communication is further broken down into verbal and non-verbal in Table 4.

The hospital ideologies technique was administered to 50 patients, selected at random from all wards of the hospital, with no consideration as to age, sex,

TABLE 3

Subdivisions of Responses in Category "The Art of Nursing," to Indicate General and Specific Qualities of the Nurse

Hospital Ideology	Social Personality	Communication	Total
Positive, "Good"	141	106	247
Negative, "Bad"	39	139	178
Totals	180	245	425

TABLE 4

Further Subdivision of Responses in Section "Communication," to Indicate Importance of Verbal and Non-verbal Communication to Patient

Hospital Ideology	Verbal Communication	Non-verbal Communication	Total
Positive, "Good"	27	79	106
Negative, "Bad"	57	82	139
Totals	84	161	245

TABLE 5

Miscellaneous Responses Not Bearing Directly upon Nurse-Patient Interaction, as Given by Cancer Patients with Hospital Ideologies Technique

Subsection of Miscellaneous	Positive, "Good"	Negative, "Bad"	Total
Religion	10	0	10
Family members of patient	3	0	3
Smoke, drink, swear	0	11	11
Discuss personal problems with patient	0	8	8
Attitude toward nursing profession, etc.	7	18	25
Totals	20	37	57

site of illness, or social status. The patients were told that the nursing department wished to improve nursing care, and would like an evaluation of the service the patients were receiving to assist in planning a more effective program. The answer sheet was not to be signed, thus providing personal anonymity, if the patient so desired. The patients were instructed to complete the blank without conferring with other patients. The three areas of the technique having to do with general, specific, and the ideal nurse were pointed out.

RESULTS

A qualitative survey of the consistent responses given by the majority of the patients preceded a quantitative analysis into meaningful categories. The qualitative overview revealed three divisions of responses. First, a large number of

the items listed in all three areas under consideration had to do with routine nursing skills and descriptive phrases connected with the physical well-being of the patient. A second division, involving an even larger number of items in all three areas, seemed to bear upon psychologic skills and descriptive phrases conducive to the emotional security of the patient. A few items did not fall into either of the two major headings; the number was so small that it was decided to group them in a miscellaneous category for further study and subdivision. After careful reconsideration of the responses collected in the three tentative sections, definitive categories were set up for final tabulation of the data.

In the category labelled "communication," an interesting indication is to be seen in Table 4. Although verbal communication between nurse and patient seemed highly important, non-verbal communications—transmitted through feeling tones, attitudes, and voice—was even more significant to the patient. Verbal communication emphasized the necessity for a two-way exchange of thinking and feeling. The patient not only wanted the nurse to talk to him, but also wished her to listen to his account of his needs as well. Under non-verbal communication a smile, a manner that put the patient at ease, a feeling that the nurse was interested in him as a person, and impartiality toward all patients were deemed paramount.

The "Miscellaneous" category contained 57 responses which did not fall into the meaning of the two common divisions. These items included several distinct subdivisions. Table 5 depicts a quantitative analysis of these data.

DISCUSSION

There is a consensus among authorities in the field that the nurse-patient relationship is one in which the patient has a heavy emotional investment because of the unaccustomed dependency situation. No single motivation could possibly be said to account for the subtle exchanges of feeling and reaction mutually aroused in such situations. What the nurse says and does and the way she says and does it, become fraught with emotional connotations resulting from a combination of the patient's anxiety concerning his disease and adult frustration engendered from dependency. The analysis presented here of the responses of 50 hospitalized patients indicates that their emotional needs and expectations in the nurse-patient relationship are significantly greater than their expressed concern about physical care. This does not mean that the patient ignores or belittles basic scientific competence and care as rendered by the nurse. It does suggest that he rather routinely expects nursing care conducive to his physical comfort, and that he becomes aware of this aspect of nursing only when it is lacking. This was highlighted in the patient protocols by the repetition of the desire for promptness on the part of the nurse, and the frustration ensuing when it was absent. The concentration of responses in the area concerned with psychologic skills of interpersonal relations, however, seemed not only to emphasize the deep need for emotional reassurance from those who care for the patient in the dependency state, but also to pinpoint the nurse's need for added proficiency in interpersonal skills.

From the patient's point of view, what are the ingredients of good nurse-patient relationships? Interpretation of the responses from the 50 patients of the research sample suggests three specific and major qualities of the nurse conducive to emotional security of the patient in this critical interpersonal reaction. First, the attitude of the nurse must be one of empathy more than of sympathy. Second, the personality of the nurse must be one of warmth and cheerfulness. Third, communication between patient and nurse must be free and easy at the verbal level, and warm and reassuring at the non-verbal levels. Fourth, promptness is an outstanding virtue. Each of these factors bears elaboration.

1. Empathy, not sympathy

Perhaps more than any other one nursing skill, the patients' expressed need was for that intangible quality called empathy. It was interesting to note how clearly the patients' statements defined empathy and rejected sympathy. Seventeen individuals made specific elaboration of this theme, as follows: The nurse should "be able to put herself in the patient's place," "feel about the patient as herself," "treat patient as she would like to be treated," "feel no better than the sick one," and "feel genuine interest in patients as people." One patient actually expressed the urgent emphasis on the "art" of nursing by saying, " a nurse should never lose close contact with the bed-patient; if she does, nursing becomes just a science and too much is lost." Another said it a little differently; "a nurse should never become hardened to human suffering; she loses the key to her nursing right there."

That this desired quality of empathy differs from sympathy in the thinking of the patient is substantiated by the quotations from the protocols on the subject. A few illustrations follow:

It's good to feel sympathetic, but there's such a thing as too much sympathy.

Feel sympathetic, but don't overdo it.

Never pity a patient too much.

A nurse should not have that "I feel sorry for you" attitude all the time.

Be sympathetic without demoralizing the patient or his family.

The most potent emotional need, then, would seem to be filled by a nurse who identifies herself with the patient, who never becomes hardened to human suffering, who "never forgets that humankind is made up of individuals, each important to himself," and who has the ability to convey that feeling to the patient without his interpreting it as pity rather than empathy.

2. Personality

The nurse's social personality plays an important role in the nurse-patient relationship, and may be either a valuable asset or a decided liability. What are the personality attributes emphasized as "good" by the patients?

Personal *warmth* and *cheerfulness* were stressed by the patients in the experimental sample. A warm, friendly, kind person was described over and over in the protocols. It was as if the patients sensed that it was the nurse who set the emotional climate on the ward, and felt secure or anxious according to the barometer

of her personality. It is evident from the following illustrative excerpts, that the patients realized that the nurse's behavior is not always determined only by her scientific skill and knowledge, but also by the way she is affected by the patients, their symptoms, complaints and diseases. They seemed to be pleading for understanding.

Never dislike a patient whatever his personality; never forget he's sick.

Overlook patient's faults, as much as possible.

Be a little understanding in all situations, though it's hard sometimes with so many duties. Realize patient's crankiness may be due to pain or fear.

Don't expect patient to be perfect.

Never be too sure the patient is cranky instead of uncomfortable.

Kindness from the nurse seemed a major need if the patient was to feel any degree of emotional security in the hospital setting. The descriptive adjective "kind" appeared in practically every protocol. Elaborations on the term seemed to indicate that the patients yearned for an atmosphere permeated with the warmth and security of the child-mother relationship. Even sibling rivalry seemed to be present. They repeatedly gave such responses as the following:

Not be impatient; treat all patients alike.

Think ahead for things which ease the patient's discomfort.

Ask if there is anything else they can do.

Be kind and treat all alike.

Be considerate of her patients.

Unselfish, and thus willing to do the little things her job doesn't demand.

Be kind to every sick person.

This desire for a mother-figure in the dependency situation was also evident in the description of the need for a *friendly* nurse. One patient seemed to express the doctor-nurse-patient triad as a substitute mother-father-child situation as follows:

Remember she is the counterpart not only of the doctor's world, but also the patient's world. Seek to enhance the relationship between doctor and patient.

The home-wish was evident in such items as the following:

Make a patient feel at home.

Help the patient be satisfied during stay at hospital.

Begin immediately to make patient comfortable and at home.

A *cheerful* nurse was a unanimous desire. Thirty-four times such phrases as "greet the patient with a smile," "a sense of humor," or just "smile" appeared in the responses. Others waxed more eloquent and expressed a desire for a nurse who would "radiate happy and cheerful attitudes"; or, even more specifically, one patient said, "I want the nurse to be cheerful because she believes in hope . . . synthetic cheer is worse than none." Still another stated, "never lose sight of the miracles she has seen . . . that is, never lose hope."

These responses furnish greater insight into the rejection of sympathy by the patients. It is almost as if they fear that too great evidence of sympathy is a foreshadowing of impending death upon which they do not wish to dwell. It is as if they hunger for laughter and light interchange of banter as a means of reas-

surance. They seem to be telling themselves, "as long as my nurse is smiling and joking, I must be getting along all right." In an atmosphere of warmth and cheer, the patient seemed to feel they could find courage to fight back, whereas "too much pity" or sympathy demoralized them and their family members. This atmosphere of brightness and cheer contributed greatly to their expressed sense of well-being and hope.

3. Communication

Non-verbal. The need to communicate with the nurse has been stressed in the desire for empathy and the warm cheerful personality. This communication is mostly non-verbal, and is picked up in the feeling tones and attitudes of the nurse as sensed by the patient. The ill person seems to be almost uncanny in his skill at "picking up" the signals of this non-verbal communication. The anxiety and enforced dependency experienced from illness and hospitalization often tend to make the patient extra-sensitivite to feeling tones, and sometimes misinterpretation of the nurse's attitude creates unnecessary tension and distress for the patient. If the nurse is aware of the great need for the emotional reassurance furnished by her interest and steadfast responsibility for her patient, she can often avert personality difficulties and ward off conflicts. As the mother-figure, the nurse is, as one patient put it, "the most important person in a hospitalized patient's life." If she makes the patient feel he has individual attention, thinks of the reasons why the patient is irritable, has real patience and compassion, realizes that the patient's irritability may be due to pain or fear, and transmits these feeling tones and attitudes to the patient through her manner and voice, her skill in nonverbal communication is beyond reproach.

Verbal communication is also of the utmost importance to the patient. This is a two-way system in which the patient wishes the nurse not only to talk to him, but also to "listen and try to understand." So often in this study, the patients seemed to feel that they could not question the doctor about their disease, their length of stay in the hospital, and other items of intense interest to them because the doctor was "too busy." The closeness that develops through physical contact necessary to care for a bed-patient makes the nurse seem much more accessible. She is, as one patient has said, "the counterpart of the doctor"; therefore, the patient feels that she knows the answers to his questions. He yearns to have her talk to him, answer his questions, and make him feel free to ask questions. This freedom for communication is facilitated when the nurse "introduces herself," pays a compliment, and is a good conversationalist.

What do the patients want from this communication? They want the nurse to tell them "how and why." One patient reported that he had refused an operation because he could not see how such an operation could be performed. Another refused hemipelvectomy for sarcoma because he did not understand why such drastic surgery was necessary. The doctor had explained, but the patient needed someone to discuss it with him who would use words of his own vocabulary, and who could more or less draw him a picture. The nurse is expected to persuade

rather than force the obstinate patient to accept a certain type of treatment, to help patients understand why it is important for them to stay in the hospital, and to be satisfied while they are there, to "joke" with them and "encourage" them.

Not only do patients want the nurse to talk and explain things to them, but they urgently need to feel that the nurse is going to listen to their objections and complaints, and "listen and try to understand" when they complain of "pain". Communication skills of the nurse, then, should include not only easy accessibility for questioning and reassurance verbally, but also the art of listening.

4. Promptness

Any discussion of the needs and expectations of the patient in the nurse-patient relationship would be incomplete without consideration of the one major complaint expressed by the sample investigated. To be prompt was the highest compliment a patient could pay a nurse and, conversely, lack of promptness was the unpardonable sin. One patient expressed the consensus of all when she said, "be as prompt as she can; minutes are hours when you are in pain." Still another exploded a particular frustrating personal experience by admonishing, "answer bell promptly; don't leave patient on bedpan until they grow to it!" Every patient of the sample listed promptness in one way or another as one of the greatest virtues of nursing care. This concentration on one item would seem to indicate that some thought should be given to expediting delays in patient care.

SUMMARY

An investigation of the expressed needs and expectations of 50 subjects chosen at random as to age, sex, site of illness, or social status from a group of cancer patients has been presented.

The patients of this research sample indicated that they had four definitive needs above and beyond what might be termed routine nursing care. Only one of these needs had to do with scientific care (promptness). The other three were concerned with the nurse's skill in psychologic management, *i.e.*, the "art" of nursing. Quantitative analysis of the data suggests that the patients of this sample needed and expected the nurse to:

1. Be prompt in caring for physical discomfort.
2. Create an emotional climate of warmth and cheer on the ward.
3. Build a bridge of rapport across which the feelings and anxieties of the patients might flow unhampered to the nurse for reassurance and explanation.
4. Give emotional support when the going got rough, holding out to them the miracle called "hope," and serving as liaison between the patient and the doctor.

The patients felt that these four needs might be filled by the nurse through empathy rather than sympathy; through those intangible personality qualities

known as warmth, kindness, and bright cheerfulness; through verbal communication; and, even more, through non-verbal feeling tones and attitudes.

REFERENCES

1. Bernstein, L.; Brophy, M. L.; McCarthy, M. J., and Roepe, R. L.: Teaching nurse-patient relationships: an experimental study, *Nurs. Res.* **3:** 80 (Oct.) 1954.
2. Robinson, A. M.; Mellow, J.; Hurteau, P., and Fried, M. A.: Research in psychiatric nursing. III. The psychiatric head nurse, *Am. J. Nurs.* **55:** 704 (June) 1955.
3. Weisman, A. D.: The doctor-patient relationship: its role in therapy, *in* Case Histories in Psychosomatic Medicine, edited by Miles, Cobb, and Shands. New York, Norton, 1952.

CARE OF THE TERMINAL CANCER PATIENT*

J. HERBERT NAGLER, M.D.**

Philadelphia†, Pennsylvania

The search for a cure for malignancy occupies an important place in the public mind and may be successful in the near future. Meanwhile, however, patients are suffering with and dying of malignant disease, and require good medical attention now. This is chiefly a problem for the general practitioner, because these patients are usually longest under his care.

The indiscriminate prescription of narcotics when terminal cancer is diagnosed falls far short of adequate therapy. The patient may not even need narcotics, but he will need general care. The family physician can make a tremendous contribution to the cancer problem; no huge research sum is required. The rules and methods that must be applied to terminal cancer patients are familiar, but are often neglected because the physician experiences a sense of futility. He is unable to effect a complete cure, and objects to striving for a lesser goal. Much of the literature on the subject has been contributed by theologians and social workers, but instructive scientific articles are available (1–11).

Patients afflicted with terminal cancer may be active and apparently healthy for months or even years. The diagnosis is not precise, but purely relative. It implies that these individuals have received the maximum benefit of surgery and irradiation, but it furnishes no information as to their anticipated years of survival. During this period they must be cared for like anyone else. Their ailments may be quite painful or incapacitating, but may nevertheless be amenable to routine therapeutic measures, whether or not they result from malignant disease.

DIAGNOSIS

Diagnosis consists of confirmation of the presence of malignancy and determination of whether or not all of the patient's complaints are related to the basic disease. The first step must include tissue microscopy if at all possible, because no other diagnostic method, no matter how obvious or certain, is acceptable. Particularly today, when so many of the granulomatous lesions are amenable to specific therapy, a pathologic diagnosis is mandatory. This is illustrated by the case of a young man, about 30 years of age, who was admitted in December 1953, from the Orthopedic Service of a Philadelphia medical school. Osteogenic sarcoma of the tibia with multiple metastases to the lungs had been diagnosed. The patient was bedridden, and had a life expectancy of one or two months. Six to twelve doses of morphine or a substitute daily, and sedatives in addition, were being given. A foul-smelling ulcer, measuring about 5 by 10 centimeters, pene-

* Presented at the Inaugural Meeting of the General Practice Section of the Medical Society of the State of Pennsylvania, Pittsburgh, Pennsylvania, September 22, 1955.

** Associate in Oncology, Albert Einstein Medical Center, Northern Division; Associate in Medicine (Geriatrics), Hahnemann Medical College, Philadelphia.

† Address: 5517 Greene Street, Philadelphia 44.

FIG. 1. Roentgenogram of lower legs in a case inaccurately diagnosed as sarcoma of the tibia.

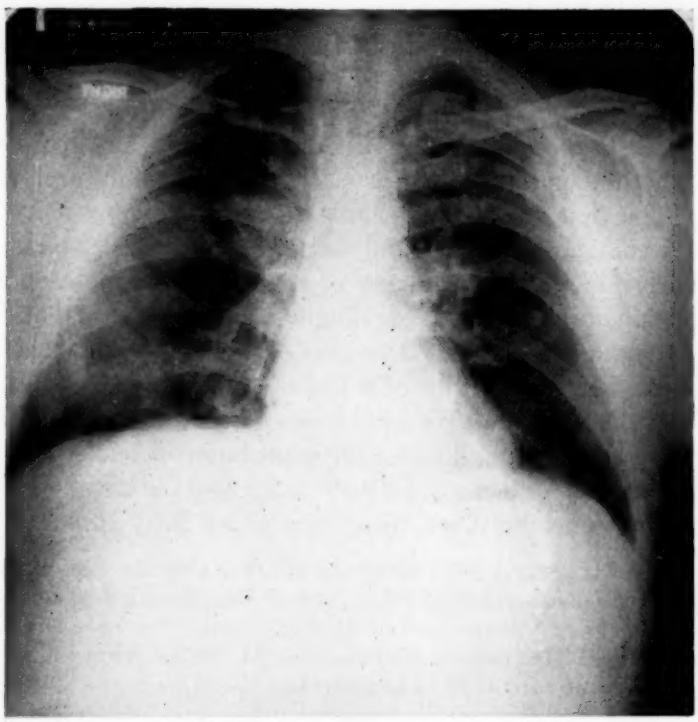

FIG. 2. Roentgenogram of the chest. Findings had been diagnosed as multiple metastases to the lungs from a sarcoma of the tibia.

FIG. 3. The patient whose admission roentgenograms are shown in Figures 1 and 2. This photograph was taken twenty months later.

trated into the bone marrow on the anterior surface of the right lower leg, just below the knee. Roentgenograms of the lower leg and of the chest are shown in Figures 1 and 2, respectively. Narcotics were withdrawn rapidly. Within two weeks, the patient was out of bed, and within six weeks, he was standing. Figure 3 shows his appearance twenty months later. Figure 4 represents the corresponding chest film. The patient improved remarkably and evidence of the sarcoma disappeared. No one visualized a more serious disease than a giant-cell tumor of doubtful malignancy in the tibia; the previous diagnosis of sarcoma had been made strictly on clinical and radiologic grounds. A biopsy of the chest lesions was not made because these lesions had started to disappear, without treatment, by the time the accuracy of the diagnosis became suspect. Figure 5 shows the appearance of the leg lesion twenty months after admission. A biopsy specimen was taken two months later from an area of the base; it was found to be necrotic granulation tissue. The deterioration in the patient's condition at the time of admission had occurred, not because of cancerous disease but because of the administration of large doses of narcotics.

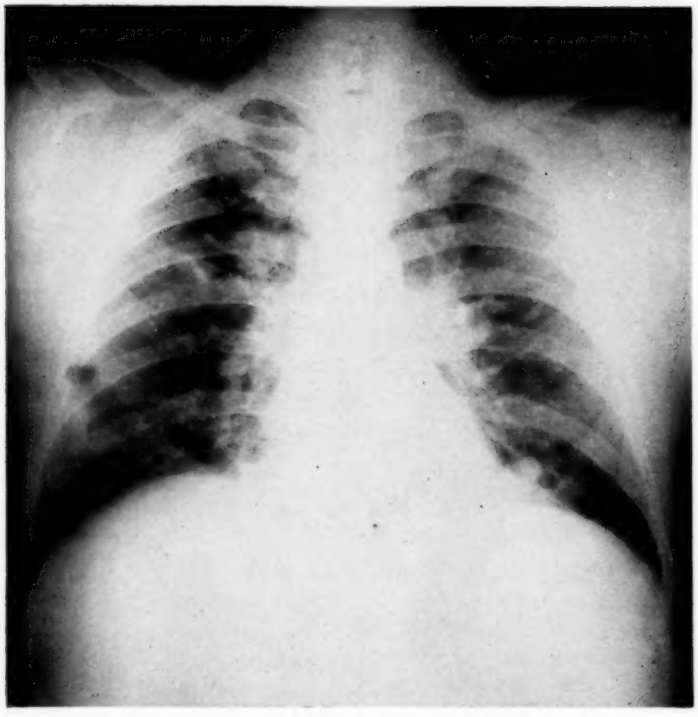

FIG. 4. Roentgenogram of chest, taken at the time of the photograph in Figure 3, showing reduction in size of lesions.

FIG. 5. Close-up of healing ulcer shown in Figure 3.

The second phase of diagnosis—determining whether or not individual symptoms are related to the underlying malignancy—may require considerable study. Is the edema of malignant or of cardiorenal etiology? Does the pain originate in cancer-affected areas, or is it due to some unrelated condition? Are anorexia, weight loss, and changes in bowel habit actually the result of the malignancy? Questions like these must be answered in order to make the diagnosis complete.

Edema of the extremities may mimic the results of metastatic involvement of spinal nerves; fluid in the chest or abdomen may simulate solid masses. Many of the patient's complaints may be due, not to the tumor itself, but to irritation or secondary infection. Hollow organs, and in particular the gastro-intestinal tract, may become irritated and secondarily infected by the continual passage of contents, thus making the primary tumor seem larger.

TREATMENT

Treatment is best begun with an intensive effort to eliminate narcotics. This is imperative, because in almost every case it will be found that either the physician, the nurse, the responsible family member, or the patient has instituted a schedule of overdosage with oral or parenteral pain killers. Narcotic addiction itself causes anorexia, malaise, weakness and, not infrequently, abdominal pain or cramps. Often these symptoms are incorrectly attributed to the malignant process. The patient may have become an addict, not to a specific narcotic, but to drug-induced pain relief. Weaning him from his addiction may be hampered by the physician's sense of futility. "Why," he may ask himself, "deprive the patient of this bit of relief?" The answer is that almost every patient will feel better, not worse, after he is free of the narcotic. Consumption is best reduced by using progressively smaller doses, at progressively longer intervals. Often atropine is added, and finally sterile water or an oral placebo is administered. After a period of a week or two, the patient should be told that he needs no pain killer. This frequently results in considerable psychologic improvement.

The relieve of pain can be achieved in ways other than by the use of narcotics. Nerve block or local anesthesia of tender areas may be of great value, alleviating pain without inducing depression. Cold also is worth trying. Ice bags applied directly to the painful area frequently decrease pain in a matter of minutes. If possible, the ice bag should be used continuously. When more intensive application of cold is attempted, a small dose of narcotic or sedative will prevent discomfort during the early phase of the chilling process. The entire body or an involved part can be immersed in crushed ice for varying periods of time, according to the principles introduced by Temple Fay of Philadelphia (4, 5, 11). A very convenient method of applying refrigeration is now available in the Thermorite machine. With this device, the temperature of all or a part of the body can be lowered almost to the critical level of 72°F. Remarkably long-lasting relief from pain may result. This method, although used in surgical procedures since its introduction almost two decades ago, has not been used often enough for its intended function of giving relief to terminal cancer patients.

A pathetic aspect of the terminal cancer problem is the foul-smelling or superficial ulcer, which has a typical appearance and odor, regardless of the underlying pathology. Not only does this odor disturb the patient, but it frequently antagonizes prospective visitors. Treatment begins with cleansing. The areas are gently cleansed with soap and water, and then covered freely with crystals of urea. If necessary, the ulcer boundaries are masked with vaseline or aluminum paste. Urea causes liquefaction of the ulcer debris, which can be removed by further washing. None of the newer debris solvents, such as streptokinase, streptodornase or trypsin, has been found more effective. When the superficial debris has been removed and granulation tissue appears on the surface, the area is painted with 5 or 10 per cent silver nitrate daily for about a week, and then urea crystals are reapplied. Should any of the local procedures be too uncomfortable, the area may be chilled with an ice bag for fifteen or twenty minutes before treatment. Secondary infection is treated by appropriate antibiotics. Application of this method for several months may result in healing or remarkable improvement in a huge, ugly ulcer.

Figure 6 shows the improvement which took place in a bed sore which initially was the result of an overzealous cordotomy to relieve the pain of a metastatic carcinoma of the cervix. The patient is paralyzed from the waist down; on admission, about a year before this photograph was taken, the ulcer penetrated to the bony spine.

The odor remaining after treatment with urea may be quite distressing. Often it can be eliminated merely by changing the dressings frequently but, if persistent,

FIG. 6. Healing bed sore. On admission of the patient, one year previously, this ulcer had penetrated to the bony spine.

it may be adsorbed by animal charcoal prepared in small sachets about 4 inches square. These are kept close to the offending area for six to twelve hours and then allowed to air for twice as long. About six such sachets, used two at a time, will help greatly in reducing obnoxious odors.

Fluid, either interstitial or in normal body cavities, must be removed if at all possible. Oral or parenteral diuretics should be tried first. Edema of the extremities, such as in an arm following radical mastectomy, may be relieved by the application of an elastic, nonadhesive (Ace) bandage; this should be removed and reapplied whenever it becomes loose—perhaps every four to six hours at first. Even the fingers can be bandaged individually if necessary, but rarely the toes. For as much of the time as possible, the edematous part should be elevated, even if only by 2 or 3 inches. The patient may even remain in bed for a day or two to facilitate elevation.

Fluid in the pleural and peritoneal cavities should be removed as often as is necessary. Occasionally the process of accumulation suddenly slows down or stops completely. One patient with lymphosarcoma, who had more than 50 abdominal paracenteses in the second last year of her life, lived for a whole year after the last tap was required. A recent post-mastectomy patient required six thoracic paracenteses from two to six weeks apart. Each yielded 500 to 2,600 cc. of fluid. Yet during the last ten months of her life no tap was required, because she again responded well to mercaptomerin sodium (Thiomerin®).

Incontinence of urine should be controlled by a Foley catheter, and incontinence of feces by the administration of paregoric or a similar substance.

The integrity of the unbroken skin should be maintained. "Doughnuts" of soft material should be applied at pressure points, both before and after sores develop. When the skin becomes redder than usual, it needs immediate care. Minor sores should be treated with generous applications of equal parts of castor and cod liver oils, or of cod liver oil mixed with zinc and magnesium oxide (Desitin®).

More specific therapy is directed against particular neoplasms. When a specific is used, the dosage should be adequate. Estrogen in the form of stilbestrol, 10 mg. three times a day orally, affords palliation in about 80 per cent of prostatic cancers and in many of the sex-related cancers in older women. Testosterone propionate, 50 mg. intramuscularly every two days, will help most patients with carcinoma originating in the breasts, ovaries, or the cervix. Nitrogen mustard (9) may be of benefit in the lymphomas, and radioactive iodine or drugs of the thiourea group in thyroid malignancy. Recently, hydrocortisone in a dosage of 25 mg. three times daily by mouth, has been used with an excellent subjective response; the subjective improvement may have a highly beneficial effect upon the objective condition. Substances formerly used but now only occasionally administered include cobra venom and members of the pteroyl group. The only thing approaching a magic cure seems to be TLC, or tender loving care, which may be of amazing benefit to the terminal cancer patient.

None of these procedures cures the cancer. However, any of them may make the patient feel better, and may even prolong his useful life. In cases in which

some specific, such as a steroid, inhibits the disease for months or years, it may be difficult for even the critical physician not to become overenthusiastic.

Continual re-evaluation of the patient's condition is imperative. The general practitioner should restudy the patient at least monthly. Frequently when the surface debris has been removed from a lesion, it is desirable to have a re-examination by the radiologist and surgeon. When a patient's life has been extended for an unexpected number of months, it may be that he has lived longer than the originally calculated tissue tolerance to irradiation, and is again eligible for treatment. Moreover, the surgeon may reconsider his decision not to operate when he sees a more circumscribed lesion in more healthy surroundings. It must be remembered that irradiation and surgery still are the only means by which cancer can actually be destroyed.

Less technical aspects of therapy deal with the psychology of the patient. The patient should continue to be ambulatory and remain at home as long as his presence does not cause undue difficulty. Natural, everyday foods are preferable to food supplements, no matter how tasteful. Ice cream, hamburger, and fruit juices may provide all of the nutrients necessare over a long period, yet they pass with relative ease through an almost completely closed esophagus. Parenteral medication should be held to a minimum.

Intelligent nursing is most important. The responsibility for guidance in this respect falls largely or entirely upon the physician. Even in nursing homes, he is not absolved of responsibility. The personnel changes frequently, and orders given to a nurse one day may mean nothing if a different nurse is on duty the next day. Because so many practical nurses are being utilized, the physician should be specific in his directions; for instance, an order should not be "Routine colostomy care," but "Aluminum paste around wound area every day."

The surroundings of a terminal cancer patient need not be lonely and gloomy. Provision for companionship and pleasant environment should be made, at home or away; in fact, the possibility of such companionship may be used as a lure, if at first the idea of a nursing home is rejected. The patient should be surrounded by optimism, however false. This applies to all who are around him, but particularly to the physician. Each untoward event should be belittled or described as part of the disease. Every favorable happening, however trivial, should be exploited to its maximum. Fortunately, these patients are so willing to seize upon any sign of improvement that they actually fool themselves.

To the specific question, "Do I have cancer?," we have a varying response, depending upon the time factor. We do *not* believe that these patients want the truth; rather they want to be assured that they have no malignant disease. If they are still in the preoperative or pre-irradiative stage, we reply that the condition is not presently malignant but may become so and therefore should be adequately treated at once. If definitive therapy is already complete, we may just continue to equivocate indefinitely. This method, incidentally, was quite successful in the later months of life of both of our own parents. Our powers of ingenuity were put to a terrific test, but our efforts were completely justified.

The euphemisms "malignant tumor" or "chronic ulcer" should be substituted

for the term "cancer" when the disease is referred to in the presence of the patient. This practice, though it may seem childish to some, elicits cooperation in such matters as having wills drawn, without unduly saddening the patient. Conversely, great depression may be induced if the patient learns his diagnosis prematurely. The patient should become aware of the diagnosis only gradually, so that when he finally realizes his hopeless state he will be too tired to care.

Accurate prognosis in such a complex disease state is almost impossible, yet often must be attempted. Members of the family may have to be summoned from great distances, and this may cause physical and emotional hardship. It is probably best to keep one relative well informed, than err, if possible, on the side of optimism.

In closing, we must re-emphasize the value of tender loving care in the supervision of terminal cancer patients. Astonishing results may be achieved by such therapy. It seems impossible that cancer, probably the least psychogenic of all diseases, should be affected by the emotions, but it is. The function of the physician is not merely to prolong the existence of the doomed patient, but to permit him enjoyment of as much of his life as possible.

REFERENCES

1. Bonica, J. J.: The management of cancer pain, *GP* **10:** 35 (Nov.) 1954.
2. Brown, R. L.: Management of the patient with incurable cancer, *South. Med. & Surg.* **113:** 371 (Dec.) 1951.
3. Daland, E. M.: Palliative treatment of the patient with advanced cancer, *J.A.M.A.* **136:** 391 (Feb. 7) 1948.
4. Fay, T.: Observations on prolonged human refrigeration, *New York State J. Med.* **40:** 1351 (Sept. 15) 1940.
5. Fay, T., and Henny, G. C.: Correlation of body segmental temperature and its relation to location of carcinomatous metastasis. Clinical observations and response to methods of refrigeration, *Surg., Gynec. & Obst.* **66:** 512 (Feb.) 1938.
6. Goodman, J. I.: Care of the chronically ill, *Ohio State M. J.* **44:** 1205 (Dec.) 1948.
7. Jordan, R. E.: The art of medicine and the cancer patient, *J. Kansas M. Soc.* **55:** 252 (May) 1954.
8. LaDue, J. S.: The management of terminal patients with inoperable carcinoma, *J. Kansas M. Soc.* **54:** 1 (Jan.) 1953.
9. McCarthy, J.: The palliation and remission of cancer with combined corticosteroid and nitrogen mustard therapy, *New England J. Med.* **252:** 467 (March 24) 1955.
10. Pendergrass, E. P.: What to do for the cancer patient when he returns home. The role of the radiologist, *J.A.M.A.* **137:** 1585 (Aug. 28) 1948.
11. Smith, L. W., and Fay, T.: Temperature factors in cancer and embryonal cell growth, *J.A.M.A.* **113:** 653 (Aug. 19) 1939.

MORBIDITY AND MORTALITY IN OLD AGE.

A Study of Experience in a Modern Home for the Aged. Part II*

ISRAEL GITLITZ, Dr. P.H†.

New York, N. Y.

THE HOME FOR AGED AND INFIRM HEBREWS OF NEW YORK

The data for this study were obtained from the medical records of the Home for Aged and Infirm Hebrews of New York.

The Home was opened in May 1870 to meet the growing needs of one segment of the aged population of the New York City area. In the words of the founding group, the B'nai Jeshurum Ladies' Benevolent Society, their intention was to establish "a home for aged and infirm persons of the Jewish faith and for the purpose of relieving all deserving Jewish applicants who may be considered by its officers worthy of Society's bounty." From a population of 4 women in 1870, the Home grew to a bed capacity of 910 in 1952 (84). Altogether, in 1951, the Home served more than 1,000 aged persons, of whom almost 40 per cent were 80 years of age or older. In that year, 3,098 persons[1] asked for the help of the Home, but only 201 could be admitted.

Services of the home

The Home provides facilities for able-bodied individuals as well as for the acutely and chronically ill and the handicapped. It maintains arrangements with Mount Sinai, Lebanon, and Bronx Hospitals, so that persons needing special care may be readily transferred to one of these institutions. In addition to providing for the persons housed in its facilities, the Home conducts an extramural care program, serving about 60 persons; this program provides medical care, nursing service, social service and housekeeping aid to the aged in their homes, enabling them to live in their own communities.

The medical staff of the Home is organized according to the requirements of the Joint Commission on Hospital Accreditation and is recognized by that body.

Within the past few years, a psychiatric staff has been developed. The nursing staff is made up of professional registered nurses who serve in directorial and supervisory capacities, and of licensed practical nurses, attendants and orderlies.

The complete physical examination of all applicants and the recording of the medical histories prior to admission were begun by Dr. Frederic D. Zeman in 1925. The medical examination given at the time of admission is followed by a

* Part of thesis presented to Yale University for the degree of Doctor of Public Health, 1955. (Part I appeared in the June 1956 issue of this journal.) This study was carried out under the auspices of the Medical Services of the Home for Aged and Infirm Hebrews of New York.

† F.A.P.H.A. Address: 2492 Williamsbridge Road, New York 69.

[1] The number of applications processed was 1,381; the number of potential applicants who were turned away either by telephone or at the registrar's desk was 1,717.

complete medical examination once a year and additional examinations whenever these are considered advisable. In the 1930's, the medical staff developed the practice of evaluating each resident and applicant, not in terms of chronologic age, but in terms of physical and mental capacity for normal living—a practice which, especially at that time, ran counter to the practice in the outside community.

In addition to occupational therapy, and recreational, cultural and religious programs at the Home, mental and physical rehabilitation programs have developed. Experimentation with new techniques and adaptation of old ones have resulted in the restoration to participation in the activities of the Home of many previously considered helpless.

A research program and teaching activities have been fostered at the Home. Studies have been made in such fields as cardiology, neuropathology and psychiatry. For the past several years, a course in geriatrics has been offered in cooperation with the Mount Sinai Hospital, under the auspices of the College of Physicians and Surgeons of Columbia University. In addition, through affiliation with the division of Nursing Education of Columbia University, the Home gives special training for nurses.

A Social Service Department was begun about twenty-five years ago. This now consists of a director and eight staff members. These workers are primarily responsible for all preadmission interviews and investigations, for maintaining contact with residents after admission, and for establishing friendly relations with the families of the residents. The social service staff cooperates with the psychiatric and medical staffs in the maintenance of the mental hygiene program.

Physical plant of the home

The Home consists of the Central House in Manhattan, the new Kingsbridge House in the Bronx, and the Apartment Residences in Manhattan.

The Central House, which is the heart of the Home, accommodates 364 residents, including 70 in the fully equipped infirmary. The Central House is a complete unit, containing its own kitchen, heating system, beauty parlor, tailor shop, library, garden, recreational facilities, occupational therapy shop, and synagogue. The newest unit (Kingsbridge House, opened in June 1950) is, like the Central House, an almost complete little community. The capacity here is 388 residents. A pavilion is included at Kingsbridge House with private or semi-private accommodations for those able to pay for long-term or short-term private care. This is available both to the able-bodied and to these requiring varying degrees of physical care.

The Apartment Residences are intended for aged persons with exhausted financial resources who do not require the medical care and supervisory services of a home for the aged. These residences are designed to provide the desired security while enabling the individual to remain an "independent" and active member of the community. The Home provides general administration as well as medical care, social service, nutritional supervision, occupational therapy, and recreational and household services as needed; but the residents of the Apartments govern themselves and pool their talents and energies in the performance

of light everyday tasks and in the planning of entertainment. The capacity of the Apartment Residence is about 150.

Financing of the home

The Home is now one of the largest voluntarily supported institutions for the aged in the country. The bed capacity is shown in Table 1. In Table 2 and Figure 1 are listed the expenditures of the Home during the twelve-year period from 1941 to 1953, and a detailed breakdown of the sources of income.

TABLE 1

The Home for Aged and Infirm Hebrews of New York

Bed complement according to functional capacity and location, as of December 31, 1951

Location	Central House (105th St.)	Kingsbridge House	Apts. 87th St.	Apts. 98th St.	Total
Apartments	—	—	136	22	158
Rooms	180	178	—	—	358
Dormitory	115	108	—	—	223
Infirmary	69	102*	—	—	171
Totals	364	388	136	22	910

* Includes Private Pavilion of 62 beds, as currently assigned.

TABLE 2

Study of the Income and Expenditures of the Home for the Aged and Infirm Hebrews of New York (105th St., 98th St., 87th St., and Kingsbridge House), 1941–1953

Fiscal Year	Census*1	Expenditures	Income					Deficit
			City of N. Y.	O. A. A. *2	Donations *3	Federation *4	Total income	
1941–42	301	206,735	22,195	7,541	29,505	82,746	141,987*5	64,784 D*6
1942–43	327	287,930	29,580	10,975	43,212	108,589	192,356*5	95,574 D
1943–44	363	282,530	43,301	11,476	53,320	114,988	223,085*5	59,445 D
1944–45	363	309,008	41,802	16,380	58,695	136,755	253,632*5	55,376 D
1945–46	367	356,959	38,594	21,401	68,070	181,328	309,393*5	47,566 D
1946–47	393	487,204	50,366	40,038	109,810	209,440	409,654*5	77,550 D
1947–48	418	628,510	93,197	57,590	146,568	258,491	555,846	72,664 D
1948–49	451	692,155	110,743	160,329	165,915	263,739	700,726	8,571 S*7
1949–50	503	753,303	108,387	193,309	211,925	252,957	766,578	13,275 S
1950–51	771	1,498,401	98,402	323,308	496,916	506,915	1,425,541	72,860 D
1951–52	838	1,757,196	115,460	454,285	628,714	501,841	1,700,300	56,896 D
1952–53	854	1,900,711	96,737	553,765	691,566	479,634	1,821,702	79,009 D

*1 = Population, June 30th of year.

*2 = O.A.A. (Old Age Assistance).

*3 = Donations from relatives, friends and others.

*4 = Federation of Jewish Philanthropies.

*5 = Years 1941–47. Total budgetary income includes an average of $30,000 per year income from investments—not applicable as budgetary income thereafter.

*6 = Deficit.

*7 = Surplus.

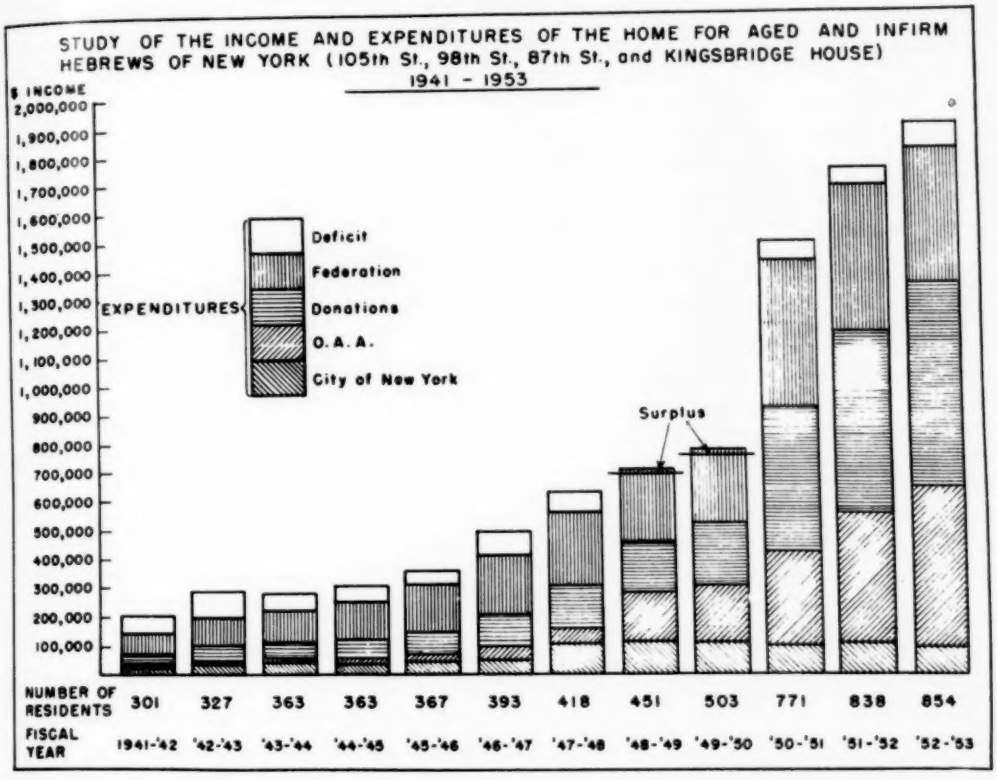

FIGURE 1

During the period 1935 to 1952, the number of employees increased from 68 to 515—more than sixfold (Table 3). The categories of employees showing the greatest increases were nurses, orderlies, and attendants. Their number increased from 16 in 1935 to 200 in 1952. During this period, total annual disbursements increased from $43,699 in 1935 to $1,757,196 in 1952, a 39-fold increase (Table 4). The major portion of the increased expenditure was for the payroll. In the fiscal year 1942–1943, the Home, with a population of 327 (119,000 resident-days care) and expenditures under $300,000, lost almost $100,000; in the period of 1951–1952, with a census of 838 (more than 300,000 resident-days care), the Home spent more than $1,750,000 with a deficit of only $57,000. Thus, although the expenditures increased nearly six-fold in a period of ten years, the annual deficit was reduced by 40 per cent.

Between 1942 and 1952, there was an increase both in residents and in expenditures, climaxed in the fiscal years 1949–1950 and 1950–1951, when the total expenditures doubled because of the addition of Kingsbridge House and the 87th Street Apartment Residences. With the increased capacity, however, the Home has increased its ability to serve the community.

In 1942 and 1943, public funds were the smallest of the three major sources of the Home's income, but by 1951 public funds had become the second largest source. From 1942 to 1947 and again in 1950 and 1951, grants from the Federation of Jewish Philanthropies were the largest of the three sources of income;

TABLE 3

Comparison of Number of Employees of Home for Aged and Infirm Hebrews, by Department, and by Selected Years, 1935–1952

	1935	1940	1941	1946	1952		
					105th St.	Kingsbridge House	Total
Engine room	Data not available	5	6	12	13	15	28
Administration		8	9	11	14	10	24
Diet and kitchen		10	10	23	31	56	87
Laundry		4	4	8	23	0	23
Other household		38	38	40	44	52	96
Nurses		7	8	23	39	56	95
Orderlies, attendants, etc.		9	9	19	35	70	105
Physicians, etc.		5	6	12	20	20	40
Social Service, etc.		2	3	4	7	4	11
Educational		3	4	5	3	3	6
Totals	68	91	97	157	229	286	515

TABLE 4

Disbursements, Home for Aged and Infirm Hebrews, for Selected Fiscal Years, 1935–1952

	1935	1940	1946	1952
Total disbursements	$43,699	$182,873	$487,204	$1,757,196
Payroll	50,124	86,596	271,633	1,052,857
Food supplies	38,053	40,370	96,159	353,767
Building maintenance	8,749	10,208	37,679	154,243
Institutional operation*	46,773	45,699	81,733	196,329
Cost per resident per day	1.12	1.50	3.26	†

* Medical, office, household and kitchen supplies; linens, bedding, wearing apparel, funerals, auditing, freight, telephone, light and power, fuel, insurance, pensions, etc.

† See Tables 5 and 6.

but in 1951 and 1952, these grants had dropped to third place. This is a good sign; it indicates that the Jewish community of greater New York is in a healthy economic state and increasingly able to pay for needed services, and that the Home, having understood the significance of this economic transition, has hastened to make its services available to residents who can afford to pay at least part, if not all, of their costs. These residents have added to the third category of the Home's three income divisions. This category also includes donations from relatives and friends of residents, and income from amortization of residents' accounts, from residents' pension benefits, and from other sources. By 1950, this category had become the second largest source of income; in 1951 and 1952, when income from the Private Pavilion started coming in, it became the largest single source of funds (Table 2 and Figure 1).

Admission policy of the home

The rules which guide the Committee on Admissions of the Home restrict admission to persons 60 years of age or older, who are residents of New York City, Nassau County, or Westchester County. Applications may be received from the individual, from his relatives or other interested persons, or from social agencies, both public and private.

Applicants to the Home may have one or more diseases or infirmities, but not active pulmonary tuberculosis or other communicable diseases; those with aggravated mental conditions are ineligible. All applicants must be medically approved by the physicians associated with the Home, and they are expected to be able to come to the Home for the required examination. Bedridden or other homebound persons are sometimes considered for the infirmary. Because it is important that applicants make an adjustment to group living, careful attention is given to their personalities. Those applying for all but the private facilities must be without resources sufficient to provide any degree of comfort or security.

At this point, it is pertinent to consider policy changes enacted and under consideration as a result of the demands made upon the Home by the community. This problem was discussed at length by R. Proskauer, President of the Home, at the Annual Meeting, October 29, 1951. At that time, he stated:

"The eighty-first chapter of the history of the Home . . . presents a picture of the development and operation of a private pavilion, and a sad story of our inability to take care of our most needy applicants.

"We have today a total of 910 beds, probably exceeding the capacity of any similar voluntary institution anywhere in the world. By the end of our fiscal year on June 30, 1952, we will have achieved a new high of 330,000 stay days, but of our bed capacity 55.6 per cent is dormitory space and 12 per cent infirmary. Due to the disproportionate size of the ambulatory quarters, the neediest (that is, the sickest) sometimes must wait three years for admission. Because of this serious problem we have cut our private pavilion space from an original 98 beds to 62, the balance being occupied by our indigent sick.

"In the distant past it was of course impossible, with the scant knowledge available in those days, to predict the problems of today. At present more and more needy aging persons desire to continue in the community as long as physical ability permits. With Old Age Assistance, and other benefits reasonably large enough to sustain him, it is natural that for the self-sufficient person independent living seems more desirable. The result is that applications from the chronically sick are increasing steadily and will become even greater as time goes on. The Home Care Program will add to our growing dilemma. Should we consider seriously the gradual adaptation of Kingsbridge House to a home for chronic sick only?"

The social pressures resulting from the increased number of persons in the upper age brackets are forcing a gradual change in basic social philosophy. Since the homes themselves are social agencies affected by this transition, they must change or cease to occupy their important position in the community. Recently

TABLE 5

Study of Average per Capita Daily Cost of Care by Individual Functional Service at Specific Locations, Home for Aged and Infirm Hebrews—Year 1952

	Central House	Kingsbridge House	Apts. 87th St.	Apts. 98th St.
Apartments	—	—	3.01	3.99
Room	4.70	5.06	—	—
Dormitory	5.62	6.39	—	—
Infirmary	9.98	9.79	—	—
Average	5.95	6.61	3.01	3.99

TABLE 6

Per Diem Cost of Operation of Room Care Service as Compared to Nursing Home Service (based on 1951–52 actual budget experience)

	Central House	Kingsbridge House
Room-care service	4.43	4.86
Nursing-home care	7.39	8.11

Formula: Census of Dormitories and Infirmaries considered as being the census of proposed Nursing Home Service, and present costs used as guide in projection.

there has been an outstanding example of such change at the Home. For eighty years, from 1870 to 1950, only indigent persons were admitted to its services. Since 1950, however, special facilities have been provided for persons who have funds, or whose families, friends or relatives can pay for their care. This is in line with the new concept that the total community and not merely one segment be served by the Home.

As indicated by Mr. Proskauer's remarks, however, another change in basic policy will soon be necessary in order to accommodate the ever-growing proportion of applicants with chronic illness who require nursing-home service (dormitory or infirmary) as against those who may require only room-care service. Studies have already been made at the Home of projected costs of such a shift (Tables 5 and 6). It seems likely that the Home for Aged and Infirm Hebrews and other similar institutions in the future will devote their institutional facilities increasingly to the care of the chronically ill.

The population of the home

This study describes the experience of 2,275 persons[2], aged 60 years and older, of whom 46 per cent were men, and 54 per cent women (Tables 7 and 8). Between 1935 and 1951, the percentage of men decreased from 55 to 40, a decrease of 28 per cent. At the same time the percentage of women increased 34 per cent. However, while the number of men relative to the number of women was decreasing, the percentage of men 75 years and over was increasing more rapidly than the

[2] The method of obtaining population is to be published later in Part IV of this study.

TABLE 7

Male Population, Home for Aged and Infirm Hebrews, by Age Group and by Time Period

Age Group	1935–1940			1941–1945		1946–1951		Total
	Population Jan. 1, 1935	New entrants	Permanent withdrawals	New entrants	Permanent withdrawals	New entrants	Permanent withdrawals	
60–64	22	9	2	8	2	16	1	60
65–69	55	37	15	21	9	36	10	183
70–74	54	58	24	35	13	86	11	281
75–79	42	42	19	37	11	112	9	272
80–84	20	25	9	18	4	75	3	154
85–89	8	9	3	12	2	37	2	73
90 and over	3	4	1	1	1	6	0	16
Total	204	184	73	132	42	368	36	1039

TABLE 8

Female Population, Home for Aged and Infirm Hebrews, by Age Group, and by Time Period

Age Group	1935–1940			1941–1945		1946–1951		Total
	Population Jan. 1, 1935	New entrants	Permanent withdrawals	New entrants	Permanent withdrawals	New entrants	Permanent withdrawals	
60–64	16	14	1	17	1	22	3	74
65–69	38	36	12	33	3	91	11	224
70–74	39	42	14	43	5	160	12	315
75–79	42	44	12	54	6	161	8	327
80–84	14	17	4	40	3	115	6	199
85–89	9	11	3	9	1	36	5	74
90 and over	3	4	1	2	2	9	2	23
Total	161	168	47	198	21	594	47	1236

TABLE 9

Population, Home for Aged and Infirm Hebrews, Percentage Composition by Sex, and by Time Period

Category of Residents	Percentage		
	1935–1940	1941–1945	1946–1951
Males in total population	55	48	40
Males 60–74 in total population	33	27	15
Males 60–74 in total male population	60	57	38
Males 75 and over in total population	23	20	25
Males 75 and over in total male population	40	43	62
Females in total population	45	52	60
Females 60–74 in total population	25	27	27
Females 60–74 in total female population	56	51	44
Females 75 and over in total population	20	26	33
Females 75 and over in total female population	44	49	56

TABLE 10

Study of the Tentative Applications Received from Applicants to the Home for Aged and Infirm Hebrews, by Sex and Time Period

Time Period	1935–1940		1941–1945		1946–1951		Subtotals		Totals
	M	F	M	F	M	F	M	F	
Applications carried over from previous years	59	52	152	184	983	1750	1194	1986	3180
New applications received during the time period	697	818	622	885	1159	1903	2478	3606	6084
Re-applications received during the time period	36	31	85	120	180	202	301	353	654
Total applications active during the time period	792	901	859	1189	2322	3855	3973	5945	9918

percentage of women in that age group, the increases being 54 per cent and 28 per cent, respectively (Table 9). The average age of the total male population studied was 75.2 years, and of the total female population, 75.1 years.

The number of females being admitted to, and residing in the Home exceeds the number of males; the women are applying for admission in greater numbers (Table 10) and are being admitted at earlier ages than are the men. Between 1945 and 1951, the total annual number of applications[3] to the Home increased about fivefold from 220 in 1945, to 1,381 in 1951. Applications from men increased from 89 to 465 (a fourfold increment); those from women increased from 131 to 916 (sixfold) (Table 10).

There are a large number of requests for applications on which no detailed statistics are kept, since they may be 1) inquiries received by telephone in the registration office, or 2) they may be applicants who are turned away if it becomes apparent at once that they are ineligible for the Home—that is, if they are not residents of the required area, if they are under 60 years of age, or if their need is not established. Applications are not accepted if the applicant is manifestly able to live in the community and does not need the Home for social and/or medical reasons. The numbers of these requests are available only for three years: 1952 (1,750); 1951 (1,717); and 1950 (1,406). Occasionally, too, at the first interview it becomes obvious that the applicant's present behavior and social history would seem to preclude an adequate adjustment to institutional life.

Nativity of the residents

A comparison of the places of birth of the 1935 and 1952 residents of the Home reveals an increase in the number of those born in Germany.[4] Thus, in 1935 German-born people represented 20.6 per cent of the total resident population, but they were 41.2 per cent of the population in 1952. In 1952, of the 376 German-born residents, 238 (63.3 per cent) were refugees, whereas of the total foreign-

[3] The Home considers an application "made" when the necessary data have been entered on the application form and signed by the applicant, who at that time is examined by the Home's official physician.

[4] Nationality study of May 1952 (Tables 11–14).

born non-German population (348) only 13.8 per cent were refugees. The refugees constituted 31.3 per cent of the total population.

The Home considers anyone a refugee who entered the United States subsequent to 1935. In December 1943, 10 per cent of the population of the Home at the Central House and 8 per cent in the Apartment Residences were refugees. It is also of interest to note that in 1943 only 10 per cent of the applications for admission were from refugees. These low percentages, both for residents and

TABLE 11

Comparison of National Origin of Residents of the Home for Aged and Infirm Hebrews, 1935 and 1952

Place of Birth	1935		1952	
	Number	Per cent	Number	Per cent
Native born	68	18.9	189	20.7
Austria	44	12.3	61	6.7
Belgium	—	—	1	0.1
Czechoslovakia	3	0.8	18	2.0
England	9	2.5	13	1.4
France	4	1.1	6	0.7
Germany	74	20.6	376	41.2
Greece	3	0.8	—	—
Holland	2	0.6	2	0.2
Hungary	47	13.1	64	7.0
Ireland	1	0.3	—	—
Italy	—	—	1	0.1
Poland	24	6.6	29	3.2
Rumania	13	3.7	15	1.6
Russia	65	18.1	134	14.7
Switzerland	—	—	1	0.1
Syria	—	—	2	0.2
Turkey	2	0.6	1	0.1
Total	359	100.0	913	100.0

TABLE 12

Refugees in the Home for Aged and Infirm Hebrews, as of May 1952, by Location

Place of Birth	Central House	Kingsbridge House	Apts. 87th St.	Apts. 98th St.	Home Care	Total
Austria	7	7	5	1	2	22
Czechoslovakia	3	1	1	0	2	7
France	2	0	0	0	0	2
Germany	78	68	59	3	30	238
Hungary	1	1	0	1	0	3
Poland	3	1	1	0	0	5
Rumania	1	0	0	0	0	1
Russia	3	2	3	0	0	8
Totals	98	80	69	5	34	286

applicants, were the rule for many years until 1950 when, with the opening of Kingsbridge House, and additional Apartment space, many more applications were received from refugees and many more were admitted.

Tables 11–14 show the national origin of the residents and their distribution by nativity group in the facilities of the Home.

TABLE 13

Distribution of Residents of the Home for Aged and Infirm Hebrews, by National Origin, May, 1952

Place of Birth	Central House		Kingsbridge House		Private Pavilion		Apts. 87th St.		Apts. 98th St.		Home Care		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Native born	80	23.8	63	19.7	16	37.2	18	13.2	6	30.0	6	10.3	189	20.7
Austria	20	6.0	24	7.5	6	14.0	8	5.9	1	5.0	2	3.4	61	6.7
Belgium	1	0.3	—	—	—	—	—	—	—	—	—	—	1	0.1
Czecho	8	2.4	6	1.8	—	—	1	0.7	1	5.0	2	3.4	18	2.0
England	6	1.8	6	1.8	—	—	1	0.7	—	—	—	—	13	1.4
France	6	1.8	—	—	—	—	—	—	—	—	—	—	6	0.7
Germany	124	36.9	112	35.0	8	18.6	85	62.5	7	35.0	40	69.0	376	41.2
Holland	2	0.6	—	—	—	—	—	—	—	—	—	—	2	0.2
Hungary	27	8.0	20	6.3	4	9.3	9	6.6	2	10.0	2	3.4	64	7.0
Italy	—	—	1	0.3	—	—	—	—	—	—	—	—	1	0.1
Poland	7	2.1	15	4.7	2	4.7	4	2.9	1	5.0	—	—	29	3.2
Rumania	5	1.5	8	2.5	—	—	—	—	2	10.0	—	—	15	1.6
Russia	47	14.0	64	20.0	7	16.3	10	7.4	—	—	6	10.3	134	14.7
Switzerland	1	0.3	—	—	—	—	—	—	—	—	—	—	1	0.1
Syria	2	0.6	—	—	—	—	—	—	—	—	—	—	2	0.2
Turkey	—	—	1	0.3	—	—	—	—	—	—	—	—	1	0.1
Total	336	100.0	320	100.0	43	100.0	136	100.0	20	100.0	58	100.0	913	100.0

TABLE 14

Nativity and Nationality of Residents of the Home for Aged and Infirm Hebrews as of May 1952

	Central House	Kingsbridge House	Private Pavilion	Apts. 87th St.	Apts. 98th St.	Home Care	Total No.	Per cent
Native Born	80	63	16	18	6	6	189	20.7
Foreign-born: in U. S. before 1936.								
Citizens	146	168	19	49	9	18	409	44.8
Non-citizens	12	16	1	—	—	—	29	3.2
Sub-total	158	184	20	49	9	18	438	48.0
Foreign-born: in U. S. 1936 or later.								
Citizens	60	60	6	66	4	33	229	25.1
Non-citizens	38	13	1	3	1	1	57	6.2
Sub-total	98	73	7	69	5	34	286	31.3
Totals	336	320	43	136	20	58	913	100.0

Rejection or withdrawal of applications

From 1935 to 1951 inclusive, 9,918 applications were received—3,973 male and 5,945 female (Table 10). In this seventeen-year period, 1,083 men and 1,937 women voluntarily withdrew their applications (Table 15). The Social Service Department turned away 1,558 males and 2,377 females during processing for such reasons as nonresidence, social and personality difficulties, under-age or failure to establish need. Ultimately, between 1935 and 1951, 1,332 men and 1,631 women were examined by the official physicians of the Home, who rejected 306 applicants (Tables 16 and 17). The chief causes for medical rejection were: incontinence and need for extensive custodial care beyond the capacity of the Home. The chief causes for psychiatric rejection were: chronic brain syndrome associated with senile brain disease (coded 009-79x) (85) and chronic brain syndrome associated with cerebral arteriosclerosis (coded 009-516) (86). The combination of incontinence with chronic brain syndrome constituted the chief joint cause of rejection.

Sixty-six per cent of all rejected applicants (Table 16) were women. Forty-five per cent of the rejected women were excluded for psychiatric reasons, and only 13 per cent for medical reasons. Men constituted 34 per cent of all those rejected. Twenty-three per cent of total male rejections were psychiatric cases

TABLE 15

Applications Withdrawn by Applicants to the Home for Aged and Infirm Hebrews, by Cause, by Sex, and by Time Period

Cause	1935–1940		1941–1945		1946–1951		Totals	
	M	F	M	F	M	F	M	F
Died	6	4	31	46	147	192	184	242
Admitted to another home	8	9	28	37	47	76	83	122
Not interested in proceeding	181	216	179	248	311	883	671	1347
Wishes kosher food	36	45	34	57	14	42	84	144
Too ill to proceed	0	1	4	3	5	7	9	11
Left state or country	0	0	1	1	5	3	6	4
Wanted special accommodations	3	4	12	17	21	38	36	59
Financial reasons	0	0	3	2	7	6	10	8
Total	234	279	292	411	557	1247	1083	1937

TABLE 16

Rejection by Cause and Sex of Applicants to the Home for Aged and Infirm Hebrews, 1935–1951

Cause	Male	Female	Total
Medical	20	39	59
Psychiatric	69	138	207
Medical and psychiatric	14	26	40
Totals	103	203	306

TABLE 17

Nativity of Rejected Applicants to the Home for Aged and Infirm Hebrews, 1935–1951, by Sex

Sex	Nativity		
	Foreign-born	Native-born	Total
Male	84	19	103
Female	169	34	203
Totals	253	53	306

TABLE 18

Comparison of Sex Differences in the Rates of Rejection of Applicants to the Home for Aged and Infirm Hebrews, 1935–1951

Sex	Number Rejected	Number Not Rejected	Total Examined	Per Cent Rejected
Males	103	1229	1332	7.73
Females	203	1428	1631	12.45
Total	306	2657	2963	10.33

$$\sigma p_1 - p_2 = \sqrt{\frac{10.33 \times 89.67}{1332} + \frac{10.33 \times 89.67}{1631}}$$

$$= \sqrt{1.27}$$

$$= 1.13$$

$$\text{Dev}/\sigma = 4.72/1.13 = 4.18$$

and only 6 per cent were medical. The overall rejection rate for men was 7.7 per cent, whereas that for women was 12.5 per cent. There is a statistically significant difference of 4.8 per cent between the two rejection rates (Table 18).

Possible reasons for the higher rate of medical and psychiatric rejection among women suggest themselves. Whereas the average age of the female applicants was 75 years, the mean age of the male applicants was 73 years; thus the women were applying for admission over a wider range of years than were the men (males, 63–90; females, 57–94).

It would seem reasonable to assume that an applicant who needs the care of a Home in the late fifties or early sixties must be showing evidence of the aging process at a somewhat earlier age than the average, or else must have some emotional problems that preclude an adequate adjustment outside the Home.

Women also apply later in life than men. It is more likely, therefore, that they would be suffering from chronic arterial degeneration with or without chronic brain syndrome.

There is more incontinence among women, with consequent need for more custodial care.

There are fewer male applicants; therefore, there is a shorter waiting period for men. When a vacancy exists, a male applicant with a borderline rejectable

disability stands a better chance of being admitted than a woman with a similar disability. Although space in general is not available in proportion to the demand for either sex, the situation is far more acute for the women.

(*To be continued.*)

REFERENCES

84. The Challenge is Greater Than You Think. Eighty-first Annual Report, Home for Aged and Infirm Hebrews of New York, 1952.
85. Diagnostic and Statistical Manual. Mental Disorders, 1952. American Psychiatric Association Mental Hospital Series, pp. 21–22.
86. *Ibid.*, p. 22.

Abstracts of Current Literature

UROLOGISCHE OPERATIONEN IM HÖHEREN LEBENSALTER (UROLOGIC OPERATIONS IN ADVANCED AGE).

Arnholdt, F. *Deutsche med. Wchnschr.* **80:** 1431 (Sept. 30) 1955.

Based on two years' experience with 4,884 patients, an attempt is made to define and evaluate the indications for, and the prognosis of, surgical intervention in old people. Preoperative treatment is of particular importance. Strophanthin or digitalis preparations are given for a few days prior to operation, even if signs of cardiac insufficiency are absent. In cases of impaired cardiac function, or if clinical symptoms of a myocardial disease are present, consultations with a physician are recommended. Patients with hypertension constitute a special risk, because they tend to have hemorrhages and circulatory collapse after prostatectomy. For these patients, light Evipan-nitrous oxide-Flaxedil anesthesia is preferred. Physical therapy, started early postoperatively, is valuable in preventing thrombotic complications. A disturbed general metabolism (by no means rare in old people, and the result of malnutrition, liver damage, or digestive difficulty) should be corrected insofar as possible before operation by means of blood or plasma transfusions, a protein-rich diet (only in the absence of marked impairment of kidney function), and vitamins B and C. It is particularly important that any disturbance in water or electrolytic balance be adjusted. In prostatism, control of the water and electrolytic balance and catheterization are often necessary. Postoperatively, it is most important that infection be diagnosed in its earliest stage and immediately treated with wide-spectrum antibiotics. A gentle technique in operating and in anesthesia will contribute to success.

ANESTHESIA FOR THE ELDERLY PATIENT.

Ausherman, H. M. *South. M. J.* **48:** 130 (Feb.) 1955.

In choosing the proper anesthetic agent and technic for elderly patients, the anesthesiologist is chiefly concerned with anatomic and physiologic changes in the respiratory, circulatory and excretory systems. The changes of senescence in the respiratory system increase the likelihood of prolonged and complicated induction of anesthesia, prolongation of the recovery period, hypoxia during anesthesia, and atelectasis or hypostatic pneumonia following anesthesia. Changes in the cardiovascular system reduce its ability to compensate during periods of stress. In the excretory system, changes in the liver and kidneys result in inefficient detoxification and excretion. Review of the patient's physical examination and the results of routine laboratory studies help in assessing the degree of physiologic impairment in the particular patient. Reassurance of the patient is important in giving him the optimistic outlook that will aid his toleration of the procedure. Premedication should be conservative, for the lower basal metabolic rate in elderly persons results in slower absorption and elimination of drugs. Supportive measures should be instituted as necessary to insure maximal physical status. In obtaining analgesia and muscle relaxation with the least physiologic disturbance, the skill and experience of the anesthesiologist are more important than the particular agent used. The technics and agents chosen are those that will provide, according to the altered physiologic findings in the particular elderly patient, the following factors in order of importance: safety for the patient, relaxation and operating conditions satisfactory to the surgeon, comfort for the patient, and convenience for the anesthesiologist. Surgical operations on the extremities can often be performed under regional or local anesthesia. The volatile agents and ultra short-acting intravenous drugs used for general anesthesia are suitable for elderly patients if smaller amounts are used and consideration is given to physiologic and anatomic changes. Low spinal anesthesia is an ideal method for many surgical procedures in the elderly patient, in that it does not affect the respiratory, cardiovascular or excretory sys-

tem. Provided that certain precautions and contraindications are observed, it can be used in such operative procedures as hip-nailing, lower abdominal surgery, vaginal hysterectomy, and prostatectomy. To make the procedure more acceptable to the patient, mild analgesia and hypnosis may be induced. The author advocates the lateral approach for spinal anesthesia rather than the conventional midline technic. Its routine use has many advantages: the patient experiences less pain; in obese patients with no palpable landmarks, the needle can be "walked" into the dural space; flexion of the spine is unnecessary; the lateral approach can be used at any level of the vertebral column; it may facilitate entry of the relatively large inflexible Huber point needle used in continuous spinal or epidural anesthesia; and no one need hold the patient in position. In the lateral approach, the wheal is made 1.5 to 2.0 cm. lateral to the midline opposite the desired interspace, and the spinal needle is advanced through it at an angle of about 10 degrees from the midline.

DISABILITY IN GERIATRICS—PREVENTION AND MANAGEMENT.

Dinken, H. *Rocky Mountain M. J.* **52:** 272 (March) 1955.

The idiopathic changes in the aged recognized as causing disability include decrease in tissue elasticity, retardation of cell division and growth, delayed tissue repair, impairment of neuromuscular reactions, decreased strength of skeletal muscle, and progressive degeneration and atrophy of the nervous system. Trauma, infection, and the immobilization required during convalescence intensify these changes. Physical agents and technics, when intelligently ordered and medically supervised, can prevent and alleviate disability through providing relief from pain, improving skeletal muscle function, maintaining range of motion in the joints, improving arterial blood flow, maintaining adequate venous and lymphatic return, enhancing neuromuscular reaction, improving gait, and insuring a maximal level of daily activity performance. Physical medicine is of benefit in the management of various medical conditions in older persons. Patients with degenerative joint disease can be taught to carry out the physical therapy part of their therapeutic regimen at home. Heat followed by massage helps to relieve pain. In patients with arteriosclerotic obliterative vascular disease, intense heat is contraindicated, but mild heat may be used directly over the peripheral joints. Exercises help to maintain mobility of the involved joints. Additional technics may be required in patients with degenerative changes. Involvement of the vertebral column may necessitate postural training and attention to weight-bearing and gait. Traction may be needed when the cervical spine is affected. In patients with rheumatoid arthritis, heat, massage, and exercise are beneficial, but more assistive and passive exercises are needed as corrective procedures when deformity is present. Fibrositis should be treated by superficial heat, massage over the involved areas, and mobilizing exercises. Patients with peripheral vascular disease are benefited by physical treatment designed to increase arterial flow to the extremities and to improve venous and lymphatic return. A patient who has had a coronary occlusion should partake of exercise suitable to his objective level of tolerance and his psychologic state. Patients with functional limitation of ventilation due to chronic bronchitis, bronchiectasis, or asthma are benefited by instruction in relaxation, breathing re-education and postural training. In patients with hemiplegia, early institution of physical treatment, which is feasible in the absence of cardiac failure or severe hypertension, helps to prevent muscle deformity and aids in muscle re-education. Physical measures and rehabilitation technics will help to prevent or correct disability in surgical patients.

ANESTHESIA FOR THE ELDERLY.

Dodd, R. B. *Am. Surgeon* **21:** 262 (March) 1955.

Deaths from anesthesia are disproportionately high in the older age groups. All elderly patients require the same care as known cardiac patients. Those with heart failure should be digitalized preoperatively. Surgery should be postponed at least for three months fol-

lowing a myocardial infarction, as the risk is increased about twelvefold. An electrocardiogram is recommended for all surgical patients past the age of 45. The prevention of respiratory obstruction may require an oropharyngeal airway, especially in edentulous patients. During anesthesia an endotracheal tube may be inserted to bypass an obstruction. Such a tube with an inflatable cuff is passed prior to anesthesia, if the intestine has not been completely depressed before laparotomy. Because emphysema and pulmonary fibrosis may be present, inhalation anesthesia is best given by semiclosed or open methods, utilizing high flows of gases. In a closed system, the to-and-fro method of carbon dioxide absorption may be preferable. Patients with liver or kidney disease can tolerate only half or a third of the adult dosage of depressant drugs. When these diseases are severe, intercostal nerve block with nitrous oxide-oxygen analgesia is satisfactory for laparotomy, but segmental spinal or continuous extradural block may be used. The measurement of blood volume is advisable preoperatively. If blood volume is deficient, several transfusions preoperatively will enable the patient to withstand anesthesia and surgery better. Even in emergencies, severe fluid and electrolyte deficits must be overcome. A dehydrated patient will withstand the rapid administration of intravenous fluids. Special considerations include the avoidance of extreme positions, and basing the duration of the operation upon the patient's general condition and life expectancy. Premedication should be light. The use of barbiturates and of morphine requires caution, as their depressant effects parallel their analgesic properties. Chloral hydrate (0.25 to 0.5 Gm.) or a short-acting barbiturate (50 to 100 mg.) usually provides adequate sedation. With general anesthesia, 0.3 to 0.4 mg. of atropine sulfate is given intramuscularly an hour prior to operation. A definite plan of anesthesia should be formulated. Low spinal anesthesia is recommended for certain procedures. The use of regional anesthesia is urged, whenever feasible, either as the sole technic or to supplement general anesthesia. The advisability of using intravenous anesthesia and relaxant drugs in elderly patients is open to question.

FIBRINOLYSIS IN PATIENTS WITH METASTATIC CARCINOMA OF THE PROSTATE GLAND.

Dolaz, E. J.; Dolehide, R. A., and Friedman, I. A. *Illinois M. J.* **107:** 142 (March) 1955.

A case report is presented of a 57-year-old man with metastatic carcinoma of the prostate gland and hemorrhagic diathesis secondary to circulating fibrinolysin. The patient had vague abdominal and leg pains of six months' duration and was bedridden on hospital admission. The bleeding-time test and the fibrinolysin test were performed after profuse bleeding occurred from the skin at puncture sites for needle aspiration. The bleeding time was in excess of thirty-five minutes, and results of the fibrinolysin test were positive. The prothrombin time was increased and prothrombin consumption was decreased. Treatment with stilbestrol, 5 mg. three times daily, was instituted. The patient was able to walk within a few days, and he was discharged on maintenance dosages of stilbestrol. Two months later he was readmitted because of progressive signs of congestive heart failure. The bleeding time was normal, results of the fibrinolysin test were negative, and prothrombin time and consumption were more nearly normal. The patient died within four months despite continued administration of stilbestrol and therapy for congestive heart failure. A discussion of the action and effects of prostatic fibrinolysin is presented. The results obtained with stilbestrol therapy may be interpreted as further evidence that the enzyme involved in fibrinolysis originates in the prostate.

INCREASED URINARY COPROPORPHYRINS FOLLOWING ACUTE MYOCARDIAL INFARCTION AND PULMONARY EMBOLISM.

Eskola, O.; Koskelo, P., and Halonen, P. I. *Am. Heart J.* **49:** 258 (Feb.) 1955.

The secretion of coproporphyrins in the urine was studied in 12 patients with myocardial infarction confirmed by electrocardiographic examination, 5 patients with pulmonary

embolism, and 12 normal subjects. The daily amounts of urinary coproporphyrins varied from 21 to 142 micrograms in the healthy subjects, who were from 20 to 60 years of age. In the 12 patients with myocardial infarction, 5 of whom were over 60 years of age, and in the 5 patients with pulmonary embolism, the daily urinary coproporphyrin secretion was increased during the first two or three days following the infarction or embolism. In the patients with infarction, the 24-hour secretion was 207 to 310 micrograms; in the patients with pulmonary embolism, it was 203 to 287 micrograms. No elevated values were observed during the second week following infarction or pulmonary embolism. The increases could not be ascribed to increased erythropoiesis, cardiac insufficiency, shock, or disturbed liver function.

PAGET'S DISEASE OF THE VULVA. REPORT OF A CASE.

Federici, P. L. *Obst. & Gynec.* **5:** 171 (Feb.) 1955.

The nineteenth case of Paget's disease of the vulva is reported. The patient was a 51-year-old female. The lesion, which was confined to the vulva, was treated by vulvectomy. Examination revealed no involvement of the underlying apocrine glands. The author postulates that the disease may arise in cells which represent embryonal rests from undifferentiated nipple tissue.

PSYCHIATRIC PROBLEMS OF OLD AGE.

Goldfarb, A. I. *New York State J. Med.* **55:** 494 (Feb. 15) 1955.

The aim in behavior disorders in the aged must be to develop, restore, or preserve comfort and self-satisfaction, make the individual productive if possible, and restrain him from aggression. The objective includes a continuation or establishment of satisfactory personal relationships and the alleviation of biologic tensions with minimal substitution and compromise. The management requires recognition that emotional and psychologic problems in the aged frequently are interwoven with severe and sometimes irreversible disease. Behavior disorders need to be examined from the viewpoint of both the internist and the psychiatrist. The physician must be alert to the possibility of emotional disease masquerading as a disorder with a seemingly physical etiology. Case illustrations deal with the occurrence in older individuals of 1) psychiatric disorders carried over from youth, 2) pathologic mourning to elicit family interest in self, 3) complaints of bodily dysfunction and pain that provided a clue to the need for psychotherapy, 4) complaints of pain, querulousness and anxiety that stemmed from a physical disorder, 5) pain that contributed to delusions and disorientation, the delusions serving as a clue to its source, and 6) a subtle change in behavior that led to the discovery of a need for special treatment. The cases show that an effective psychotherapeutic relationship can be established in elderly persons. Even when physical disability has been added to an existing emotional disorder or when emotions accentuate bodily illness in the aged, psychotherapy can be valuable. Dependency becomes a means through which pride can be engendered and strength built. The patient automatically delegates to the physician the role of parental substitute. The history-taking, examination, and diagnostic studies encourage him in delegating a sort of magical power to the physician. The patient becomes convinced that he will be helped. This reaction opens the way to self-satisfaction, which favors continued contact with reality, a broadening of this contact, and a decreased need for magical fulfillment in an aura of "parental" care. Maintaining the illusion in the aged that "parental" care and protection are continuously present and available is the goal to keep in mind; for on the basis of it, the older person may improve in performance and his suffering be decreased.

PRURITUS OF LIVER DISEASE (XANTHOMATOUS BILIARY CIRRHOSIS).

Hicks, J. H., and Mullins, J. F. *A.M.A. Arch. Dermat.* **71:** 46 (Jan.) 1955.

Generalized pruritus is caused by liver disease without jaundice more often than is commonly realized. Xanthomatous biliary cirrhosis, the most frequent cause of pruritus

of liver origin, occurs chiefly in women from 30 to 50 years of age. Six cases of this disease are reported, and detailed clinical manifestations are presented for 3 of the patients. The onset of the disease is characterized by generalized itching, with jaundice of the obstructive type developing later. The xanthoma does not appear until months or years after the jaundice has developed. The usual early findings of generalized pruritus, excoriations without primary lesions, and a mottled melasma on the face were present in the authors' patients. They had the typical early laboratory findings of a moderately elevated serum cholesterol level, microcytic hypochromic anemia, and minimal liver damage as revealed by liver function tests. Jaundice developed later in 3 of the patients. Since all were treated with methyltestosterone, whether the jaundice resulted from the therapy or from the progression of the disease was unclear. Methyltestosterone sublingually resulted in immediate cessation of the itching. Nonmethylated forms of testosterone were ineffective in this regard.

MELANOTIC FRECKLE (HUTCHINSON), MÉLANOSE CIRCONSCRITE PRÉCANCÉREUSE (DUBREUILH).

Klauder, J. V., and Beerman, H. *A.M.A. Arch. Dermat.* **71:** 2 (Jan.) 1955.

The differentiation of malignant melanoma originating in the pigmented lesion first described by Hutchinson as senile freckle or infective melanotic freckle from the more serious malignant melanoma arising from a pigmented dermoepidermal nevus is important from the standpoint of both prognosis and treatment. The authors, with frequent references to the literature, discuss the occurrence and location of melanotic freckle, the pathologic process, the prognosis, the histopathology, the differential diagnosis, and the therapy. Five case reports are presented in detail. The age range reported is broad, although the majority of the patients were in later life. The face is the area most frequently affected. The pigmented or precancerous stage of the disease, the melanotic freckle, is represented typically by a small dark brown sepia spot, which enlarges gradually and irregularly. The discoloration is not homogeneous. The tumor stage, which does not always ensue, begins as a thickening or induration of one portion of the pigmented lesion. This develops into a discrete, raised, rounded lesion, and may be single or multiple. The interval between the appearance of the melanotic freckle and development of a malignant tumor is known to vary from less than one year to forty years. When the lesion is on an extremity, the precancerous stage is shorter and metastasis in the tumor stage is more likely than when the lesion is on the face. The mortality in the tumor stage of the disease is apparently lower than that from malignant melanoma secondary to a dermoepidermal nevus (junction-type nevus). Histologic examination of specimens removed during excision of malignant melanoma should include examination of the nonmalignant portions, to determine whether or not the junction nevus cell is present. The authors employed electrodesiccation of the tumor followed by radiation therapy and electrodesiccation of the primary pigmented lesion in 2 of their patients, and surgical excision of the entire lesion followed by radiation therapy in 1 patient. In elderly patients in whom the lesion is on the face, destruction of the pigmented patch in the non-tumor stage is not mandatory. However, destruction by electrodesiccation or surgical excision is indicated when the melanotic freckle is on an extremity. Removal of the regional lymph nodes is indicated when they are involved.

SPASTIC PARAPLEGIA OF MIDDLE AGE. A CLINICOPATHOLOGICAL STUDY.

Marshall, J. *Lancet* **1:** 643 (March 26) 1955.

A review of 35 necropsy records and information from 52 traced survivors is presented in an attempt to aid the diagnosis of the underlying lesion in cases of spastic paraplegia. The syndrome is a chronic disease with a gradual onset. It progresses slowly. The average age at which symptoms appeared was 40 years in the clinical series and 43 years in the necropsy series. Among the former, symptoms appeared as early as at age 20 years and as late as at age 70. The average duration of the disease was 10.4 years in the living patients

at the time of follow-up and seven years in patients who had died. The cause of the paraplegia could be determined in 27 of the 52 traced survivors and in two-thirds of the necropsy series prior to death. It became evident in 50 per cent of the patients ten years after symptoms were first observed. Disseminated sclerosis and spinal tumor were the most frequent causes. Other causes were prolapsed intervertebral disc, syringomyelia, cervical cord lesion, Paget's disease, subactue osteitis, nontuberculous spinal deformity, hypertrophic pachymeningitis, aneurysm of the intervertebral artery, and defect in the anterior spinal artery. In 4 patients in the clinical series, dementia developed from seven to sixteen years after the paraplegia. Attention is directed to the infrequency with which cervical spondylosis is the cause of spastic paraplegia. The most helpful points in differentiating disseminated sclerosis from spinal tumor in the early stages were that 1) in all except 1 patient, the level of protein in the cerebrospinal fluid was above 100 mg. per 100 ml., whereas in disseminated sclerosis the level did not exceed 60 mg. per 100 ml., and 2) myelography showed an abnormal result in the 18 patients with spinal tumor.

PERSONALITY DISORGANIZATION AND DYSFUNCTION OF THE CEREBRAL ARTERIOSCLEROTIC PATIENT.

Milburn, A. A. *West Virginia M. J.* **51:** 73 (March) 1955.

Advanced cerebral arteriosclerosis can lead to a distortion of personality function which may reach a psychotic degree. The degree and type will vary with the type, location, and degree of the sclerotic process. The onset of symptoms may be sudden, particularly when large vessels are involved. Here, the first gross symptom may be an apoplectic stroke, epileptiform attack, aphasic attack, or other focal disturbance, but other evidence of vascular disease will have appeared first. The more slowly progressing sclerotic process seen in small vessels causes a gradual disorganization of personality function. The prodromal symptoms may be fatigue, tinnitus, headache, dizziness, and insidious impairment of physical and mental abilities. A sudden change of character in a person past the age of 50 years should suggest cerebral arteriosclerosis, if paresis can be excluded. An attack of confusion is the first obvious mental symptom in more than half of these cases. Episodes of excitement frequently are a symptom of the arteriosclerotic syndrome. The progression of symptoms in cases of involvement of the large and small vessels is outlined. The arteriosclerotic patient in the early stages of deterioration can recognize that there is a change in the speed and accuracy of his mental functions. In cerebral arteriosclerosis there may be little evidence of arteriosclerotic changes elsewhere in the body. However, the condition of the retinal vessels is a good index to the state of the cerebral vessels. As the pathologic changes in cerebral arteriosclerosis are reversible, the prognosis is unfavorable. The progression of symptoms can sometimes be interrupted by appropriate treatment such as rest and maintenance on a simple hospital regimen, so that some patients can retain considerable capacity for several years before dementia and helplessness ensue. Death is often hastened by general arteriosclerosis associated with cardiovascular renal disease. Some arteriosclerotic patients with mild psychosis can be cared for at home; those with severe personality distortion require institutional care. The fundamental requirement in treatment is a careful, well regulated mode of life. The regimen should include: avoidance of heavy physical and mental tasks and emotional stress, simple and pleasant occupation, recreation and rest, vitamin therapy, a balanced diet, and avoidance of alcoholic beverages and barbiturates. Rauwolfia preparations prove useful for sedation.

USE OF RADIOACTIVE GOLD IN THE TREATMENT OF CARCINOMA OF THE BLADDER: REPORT OF 8 CASES.

Nelson, C. M. *South. M. J.* **48:** 245 (March) 1955.

Eight patients with bladder growths were treated with radioactive gold in an effort to determine its effects on tumor cells, on normal tissue, and on the patient as a whole. A

colloidal suspension of radioactive gold was used, which was calibrated to yield 1 millicurie per cubic centimeter; and 1 cc. of solution was allowed for each cubic centimeter of tissue. When the area to be treated was large, the bladder was opened suprapubically and as much of the tumor removed as was possible. Small tumors were excised through the cystoscope. The radioactive gold was introduced into the tumor site in such a manner as to insure injection of each cubic centimeter of tissue, for gold is active only over a distance of 0.5 cm. The patients were from 47 to 88 years of age. In the majority, the treatment was used for palliation. The results indicate that radioactive gold is lethal to tumor cells when injected in adequate concentrations and that there is minimal effect on the stroma and surrounding tissues. No generalized toxic effect attributable to the gold was noted. The advantages of radioactive gold therapy include the limitation of activity to the injected area, the ease of administration, the large amounts of radio energy that can be given, and the fact that the radioactivity ceases to be dangerous within nine days after administration.

OSTEOPOROSE SÉNILE.

Panella-Casas, M.; Monteys, J.; Ferrer, D.; Manchon, F., and Hernandez, G. *Concours med.* **77:** 436 (Jan. 29) 1955.

Histologically, senile osteoporosis does not differ from the osteoporotic processes in Cushing's syndrome, the menopause, hypogonadism, and the general adaptation syndrome. Senile osteoporosis occurs more frequently in women than in men by a ratio of 5:1. Both senile and postmenopausal osteoporosis appear to be due to the same process but to differ in clinical evolution. Senile osteoporosis is an involutive phenomenon, but according to the time of its appearance and development it is probable that hormonal factors have an especial influence upon it. It seems not to be related to a derangement in calcium and phosphorus metabolism nor to hypovitaminosis D. There may be a protein disequilibrium, in the sense of a catabolic modification of the protein balance in the body of the elderly individual. Vitamin C, which plays an important part in the formation of collagen material, perhaps intervenes with respect to the deficient formation of protein matrix without there being a true avitaminosis C. In all osteoporotic processes the same pituitary-adrenal-gonadal modification apparently exists. The hormonal modifications of physiologic character that determine this involution are closely related to those that cause simple osteoporosis. Both are characterized by a predominance of catabolic over anabolic hormones as regards protein equilibrium. Senile osteoporosis evolves slowly as an asymptomatic disease with no characteristic clinical pattern. It is in itself painless, so that when there is pain it is almost always due to the vertebral complications that the disease causes. The diagnosis may be established roentgenographically. Senile osteoporosis, at least in its advanced phase, appears to be irreversible. Treatment should commence early and be prolonged in order to be efficacious. Postmenopausal osteoporosis responds in general to androgen-estrogen therapy. Its efficacy is greater the earlier the disease and the less acute its onset.

MILK-ALKALI SYNDROME. REVIEW OF EIGHT CASES.

Scholz, D. A., and Keating, F. R., Jr. *A.M.A. Arch. Int. Med.* **95:** 460 (March) 1955.

The clinical and laboratory findings in 8 cases of so-called milk-alkali syndrome are summarized. The syndrome is characterized by hypercalcemia, renal insufficiency, and azotemia and, occasionally, by alkalosis. The condition appears to be distinguishable from primary hyperparathyroidism by the absence of hypercalciuria and because of the rapidity with which the azotemia and hypercalcemia disappear on omission of milk and antacids containing absorbable alkalis. The features of this condition as they relate to the differential diagnosis of calcium disorders and to the management of patients having duodenal ulcer are discussed. (Authors' summary.)

IDIOPATHIC HYPERTROPHIC PYLORIC STENOSIS IN AN ELDERLY ADULT.

Southwick, H. W.; Slaughter, D. P., and Bollinger, J. A. *Illinois M. J.* **107:** 139 (March) 1955.

The successful treatment of idiopathic hypertrophic pyloric stenosis in an 82-year-old woman is reported. The patient's chief complaint on admission was abdominal pain accompanied by vomiting. Intermittent vomiting, becoming progressively more severe, had been present for the preceding three years. Six months prior to admission, an annular deformity in the pyloric area had been revealed by fluoroscopic examination. At operation, the involved area was resected and a Billroth I reconstruction was performed. Microscopic examination of the specimen revealed hypertrophy and hyperplasia of the pyloric musculature, with a mild interstitial chronic inflammatory reaction. The patient's postoperative course was uneventful, and she was living and well two years after operation. Idiopathic hypertrophic pyloric stenosis in the adult apparently represents a persistence of a minimal congenital lesion that produces little symptomatology until later life. Effective treatment of the condition requires surgical intervention rather than medical management, which often fails to relieve the symptoms.

THE LIVER IN CONGESTIVE HEART FAILURE.

White, T. J.; Leevy, C. M.; Brusca, A. M., and Gnassi, A. M. *Am. Heart J.* **49:** 250 (Feb.) 1955.

In an investigation of the mechanism and significance of hepatic abnormalities in chronic circulatory congestion, biochemical liver function tests and needle biopsies of the liver were performed on 75 patients with congestive heart failure. Forty-five of the patients were men and 30 were women; they ranged in age from 30 to 79 years. All the patients were on a regimen including bed rest, sodium restriction, and therapy with diuretics and digitalis. The duration of congestive heart failure was from six weeks to twelve years; the functional capacity of the patients was either Grade 3 or Grade 4. Hepatomegaly was present in 95 per cent of the subjects, ascites in 49 per cent, jaundice in 21 per cent, splenomegaly in 12 per cent, and hepatic pain in 11 per cent. Although neither the type of heart disease nor the duration of heart failure could be correlated with signs and symptoms, the occurrence of jaundice and hepatic pain was related to the acuity and severity of failure. The liver function studies showed biochemical changes in all the patients. These were most marked in patients with prolonged, severe heart failure. The biochemical data could not be correlated with the histologic findings; however, clinical abnormalities were frequently related to histologic changes. Patients with centrilobular fibrosis and diffuse fibrosis were most likely to have ascites. Jaundice was attributable to hepatocellular changes alone in 11 patients and to a combination of liver-cell dysfunction and pulmonary infarction in 5 patients. It was most intense when there was central necrosis. The serial biopsy studies revealed two ways in which liver fibrosis in heart failure may develop: a) passive congestion may lead to central necrosis and centrilobular fibrosis; (b) poor nutrition may cause fatty liver and, eventually, diffuse fibrosis. The survival periods in the patients with fibrosis or necrosis were related to the severity of the hepatic changes; in the other patients, they were related to the type of heart disease and the degree of heart failure. Patients with icterus, hypoalbuminemia, and diffuse fibrosis often had fluid retention which was refractory to therapy. The composite of clinical, biochemical, and histologic study is desirable in patients with hepatomegaly or fluid accumulation resistant to treatment.

HEREDITARY OVALOCYTOSIS (ELLIPTOCYTOSIS) WITH HYPERSPLENISM.

Wilson, H. E., and Long, M. J. *A.M.A. Arch. Int. Med.* **95:** 438 (March) 1955.

Two patients with hereditary ovalocytosis are presented. These siblings exhibited pancytopenia, splenomegaly, and bone marrow hyperplasia. One patient underwent splen-

ectomy, followed by recovery from the pancytopenia. However, numerous microcytes of various shapes appeared in the peripheral blood. Björkman's hypothesis of a divided splenic circulation seems a plausible explanation for the cytologic picture preceding and following splenectomy. (From authors' summary.)

PAGET'S DISEASE OF THE VULVA. REVIEW: REPORT OF TWO CASES.
Woodruff, J. D. *Obst. & Gynec.* **5:** 175 (Feb.) 1955.

Twenty-three cases reported in the literature that seem to fulfill the criteria of Paget's disease of the vulva are reviewed and 2 new cases are reported. The majority of the cases reviewed occurred in women over 60 years of age. The 2 patients newly reported were 50 and 60 years of age. The accumulated data indicate that Paget's disease of the vulva is an intraepithelial lesion that may progress to invasive carcinoma. The possible histogenesis of the characteristic cell in Paget's disease is discussed with reference to various theories and to the embryologic derivation of the various cells in the epidermis and associated structures. The author believes that the characteristic cells arise in the epithelium, either on the surface or in the appendages, and that the condition may be present for long periods before malignant transformation takes place. Excision is apparently the treatment of choice, and the extirpation should include a wide margin and enough of the underlying tissues to include the epithelial appendages.

NEWS AND NOTICES

THE NATIONAL SOCIETY FOR CRIPPLED CHILDREN AND ADULTS

For the first time in its 35-year history the National Society for Crippled Children and Adults will hold its annual convention at the nation's capital in 1956.

The four-day meeting of the National Society, also known as the Easter Seal Society, which will be held *Oct. 28–31* at Washington's Hotel Statler, will highlight speeches by notable authorities in rehabilitation and feature displays of newest appliances for crippled children and adults.

Among the tentative plans for the convention are a luncheon to bring together specialists from governmental and private agencies who work with the handicapped; a pageant on "Progress in Protheses and Appliances," displaying wheelchairs, crutches, braces, artificial prothesis and other equipment from 1906 to 1956; a demonstration by the District of Columbia Society for Crippled Children showing its clinical, therapy and education program, special tours of the nation's capital city, and a tea at one of the Washington embassies.

Walter Blount, M.D. immediate past-president of the American Academy of Orthopaedic Surgeons, is among the principal speakers already scheduled for general sessions planned during the mornings of the convention. Afternoons will be devoted to workshops, seminars and institutes covering many phases of rehabilitation.

James B. Johnson, M.D. prominent physician and surgeon of Newark, O., and member of the National Society's executive committee, is chairman of the 1956 convention.

Dean W. Roberts, M.D.,
Executive Director,
11 South La Salle St.
Chicago 3, Illinois.

CIBA'S "MEDICAL HORIZONS" TV SERIES TO RETURN ON SEPTEMBER 9

"Medical Horizons," Ciba's medical documentary television series will return this fall for a minimum of thirty-nine weeks on ABC-TV, it was announced today by T. F. Davies Haines, president of Ciba Pharmaceutical Products, Inc. The program will be seen each Sunday from 4.30 to 5.00 p.m., New York time, on an 85-station national network starting September 9.

Ciba's 1955–56 "Medical Horizons" series, presented in cooperation with the American Medical Association, ended on March 7 after twenty-six weeks on a network of 42 ABC-TV stations each Monday evening from 9:30 to 10:00 p.m., New York time.

"We trust that the greatly expanded coverage and continuity of the 1956–57 series," states Mr. Haines, "will inspire increased confidence in the American medical profession. We plan to have programs on advances in common everyday problems in medicine as well as on major diseases which as yet have not been fully conquered. The future of medicine looks bright, and we in the pharma-

ceutical industry are proud to have a part in the progress made toward better health."

Don Goddard, veteran newscaster, will return as narrator of "Medical Horizons." The series will again be packaged by the J. Walter Thompson Agency of New York under producer-directors Bob Foster and Bill McCarthy. "Medical Horizons" will continue under the supervision of Dr. William T. Strauss of Ciba.

During the first series, "Medical Horizons" cameras travelled over 11,000 miles to visit 26 medical centers in 20 cities located in 15 states and the District of Columbia, making it the most extensive series of remote telecasts ever attempted by any medical program. Thirty-five creative and technical people using five thousand pounds of equipment (including four miles of cable), constituted a virtual "TV Studio on the Road."

Programs were presented on the training of the medical student (University of Pennsylvania) and the doctor (Johns Hopkins), the work of the hospital nurse (Cornell Medical Center), the diagnosis and management of liver diseases (Jersey City Medical Center), the use of the heart-lung bypass (Mayo Clinic) and the artificial kidney machine (Georgetown University), the causes of headache (Duke University), the effect of temperature and humidity on the human body (University of St. Louis), the human factors in motor vehicle accidents (University of Colorado) and many other interesting medical subjects.